

# *Clinical Medicine*

## Original Articles for August, 1955

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*William Martin, M.D., Clarence Saehof, M.D.*

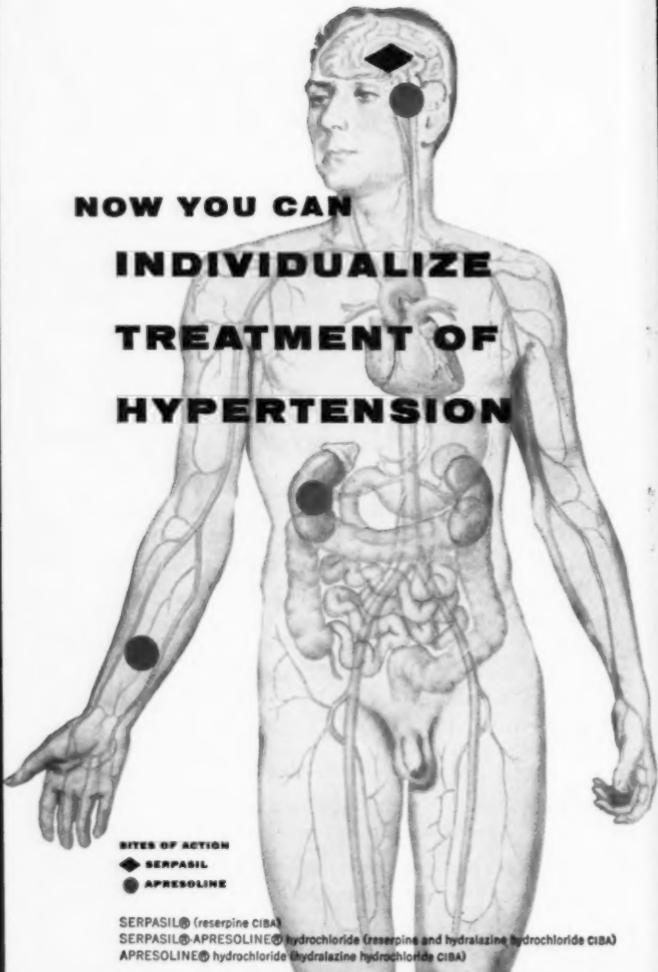
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Idiopathic Pruritis—New Etiology and New Specific Therapy . . . . . 813  
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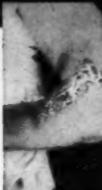
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## Treatment of Neuroses in General Practice

*Simple psychiatric treatment may be effectively directed by the general practitioner if he proceeds carefully and cautiously*

---

JAMES M. NORTHINGTON, M. D., *Editor*

While a formal psychoanalysis is probably the best method of reaching for and correcting the fundamental causes of neuroses, the very formality, rigidity and long time factor of this method renders it unavailable to most of those requiring it. A great number of psychoneurotic patients have to depend entirely upon the care of the G.P. who have been carrying these patients along in an increasingly more satisfactory manner.<sup>1</sup>

Treatment in psychiatry in recent years has been directed toward the uncovering of instinctual urges, to the recognition of specific failures in adaptation, to the unraveling of conflict situations, to helping the pa-

tient to understand the meaning of his symptoms, and to tolerate and control his emotional problems.

A complete physical and neurological examination with indicated laboratory procedures is essential. During the taking of the history and the making of these examinations the doctor has been reaching a careful evaluation of the mental state of the patient. Immediately the patient is told in simple terms the significance of all the findings in the case, correlating the various factors and outlining what is to be done. A thorough investigation on the first visit is rarely possible; complete these examinations in the next 2 or 3 days. Emphasize to the patient the doctor's understanding of the genuineness of his complaints.

<sup>1</sup> I. B. L. Keyes, *South Carolina M. A.*, Oct. 1954

Many G.P.s assign certain hours each week by appointment for these patients and charge them additionally for the time consumed. Most patients readily accept the suggestion of writing out an autobiographical sketch, if it follows assignments to be discussed by appointment. It may be well to suggest that they just make headline entries of good and bad experiences. It is surprising to discover the amount of material some patients can recall and bring forward about significant experiences which they had long forgotten.

#### GRADUAL PROGRESS

Caution should be exercised not to interpret the material too quickly. It may be possible to get him to discuss many of his accumulated hatreds and loves. The doctor must be cautious not to move forward too rapidly in any re-educational program. All patients will require repeated re-assurance, encouragement and opportunities to express themselves freely as to their emotions, their doubts, their fears, without risk of censorship, so that they may gradually discuss matters of serious moment with less and less sense of guilt, anxiety and emotional turmoil. A patient will approach a subject only to veer cautiously away from it; quietly note this, to be cautiously presented later.

When sedatives such as amyital and pentothal IV are given slowly to induce a less than fully conscious state, previously blocked-off, disturbing material may be freely ex-

pressed. Frequently it is possible to review the same situation in later sessions under less and less sedation. Occasionally reliving a previously blocked-off experience may be the turning point in recovery from the neurosis. Some patients who manifest resistance to talking out may be aided by 20 mg. methedrine with 3 1/4 grains amyital.

It will gradually be possible to develop in the patient self-assurance. Members of the patient's family will require instruction in tolerance of the patient and his symptoms and what the patient and the doctor are trying to accomplish.

#### TREATMENT AT HOME

Throughout a therapeutic program a definite sequence must be adhered to though with reasonable elasticity. Most patients should be treated on a work basis at home and on the job, rather than in a sanatorium. In every case a gradual effort must be made to re-establish the patient in some useful work.

Occasionally a few days under modified narcosis, with hypnotics allows nervous persons to get off to a good relaxing start. Insomnia is controlled by the use of sedatives, but not long continued.

Electro-sleep treatments are helpful in deep reactive depression, always under deep sedation to lessen the patient's awareness to the procedure and to minimize the convulsive reaction; 4 to 6 such treatments are usually enough.

## **Chemosurgery: A Method for the Microscopically Controlled Excision of External Cancer**

*Reliability and conservatism characterize this microscopic guidance to selective destruction of clinically undetectable cancer tissues*

FREDERIC E. MOHS, M.D., Madison, Wisconsin

A great many external cancers send out "silent" outgrowths or downgrowths which may be transected during operation or not included in the irradiated field with resultant recurrence of the neoplasm. A means by which these clinically undetectable extensions may be visualized microscopically and accurately followed to their terminations is provided by the chemosurgical method.

As the term "chemosurgery" implies, the tissues suspected of containing cancer are chemically treated and then surgically excised. The purpose of the chemical treatment is to produce fixation of the tissues *in situ* so that layers of fixed tissue may be excised for systematic micro-

scopic examination by means of frozen sections. The complete microscopic guidance of excision attained in this manner permits unprecedented assurance of cure and also makes possible the preservation of virtually all of the surrounding uninvolved tissues. Since the procedure is carried out without a general anesthetic, the risk is minimal.

### **TECHNIC**

Although the important feature of the chemosurgical method is the microscopic control of excision, there usually is a mass of grossly visible and palpable cancer which may be removed surgically prior to the institution of chemosurgical treatment. Local anesthesia is pro-

duced by infiltration of the tissues around the cancer with procaine hydrochloride. Then the visible and palpable portion of the neoplasm is removed with scalpel and curet producing a saucer-shaped depression. Bleeding is controlled by the rapid application of dichloroacetic acid\*. This chemical also is applied to a narrow zone of skin at the periphery of the defect to render the keratin layer of the skin permeable to the zinc chloride which is used as a fixative.

Fixation *in situ* is accomplished by the application of a zinc chloride paste of the following composition: stibnite, 80 mesh sieve, 40.0 gm.; Sanguinaria canadensis, 10.0 gm.; and zinc chloride, saturated solution, 34.5 cc. This preparation contains 45% zinc chloride by weight. The fixative penetrates the tissues in a controllable manner, produces satisfactory fixation, is not toxic systemically in the doses used, and has no tendency to further metastasis as demonstrated by experiments in rats.

After the fixative has been allowed to penetrate for from 1 to 24 hours, depending upon the amount of penetration desired, a layer of fixed tissue is excised with a scalpel with a replaceable blade. The incision is made through fixed tissue and not through the underlying living tissue. Hence, there is no pain or bleeding from this incision. If at this level there is no cancer which can be seen grossly, the layer of fixed tissue is systematically examined under the microscope. This is accomplished by the use of frozen sections through the under-surface of each of the flat specimens of tissue. Suitable maps are drawn on the lesion and on a pad of paper to make it possible accurately to locate any areas of residual cancer. The reapplication of the fixative then is lim-

ited to the areas in which cancer has been demonstrated microscopically. Subsequent excision and microscopic perusal determine whether more tissue must be removed. The microscopic guidance attained in this way permits the selective destruction of the cancer although the fixative chemical itself has no selective effect.

Upon completion of active treatment there remains a thin final layer of fixed tissue which separates in about a week. The resultant wound epithelializes rapidly with the formation of soft, smooth scars of surprisingly good appearance (Figs. 1-3).



FIGURE 1

Basal-cell carcinoma which had recurred after a course of x-ray therapy and after treatment with a caustic.

#### INDICATIONS

The chemosurgical method is applicable to most cancers on the surface of the body or in cavities which may be reached through normal, ar-

\*Obtainable from Eastman Kodak Co.



FIGURE 2

Granulation tissue after chemosurgical excision in 3 microscopically controlled stages. There was unexpected extension into the softer tissues of the inner canthus. Small areas of periosteum and perichondrium were invaded by the cancer.

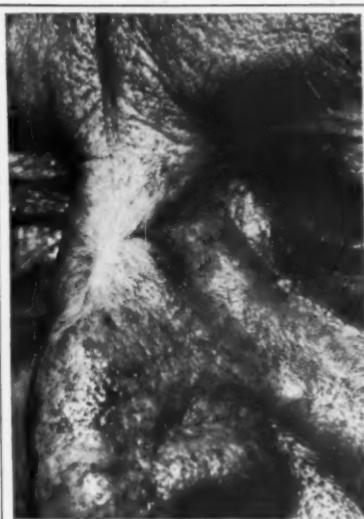


FIGURE 3

Healed lesion. There was no recurrence after 9 years.

tificial or pathologic openings. Carcinoma of the breast is not included because of the mode of metastasis; however, some lesions which have recurred after radical mastectomy may be removed chemosurgically. The most commonly treated lesions are carcinomas of the skin, lips, salivary glands, vulva and penis. Melanomas are amenable, but they should be chemosurgically excised without prior surgical excision because of the danger of dissemination of this neoplasm by the slightest trauma.

#### CANCER OF THE SKIN

A large proportion of the patients treated in a chemosurgical clinic have facial carcinomas of either bas-

al- or squamous-cell type. The microscopic control of excision is especially needed for the more infiltrative carcinomas of the nose. Not only are such neoplasms deceptive to gross visualization but they are difficult to outline by palpation, owing to the similarity in consistency of the cancer tissue and the fibrocartilaginous nasal tissues. Cancers in the vicinity of the cartilages of the nose and ears may be removed without danger of the painful perichondritis which occasionally follows treatment with radium or x-rays. Cancers of the eyelids may be treated without damage to the eye, because the edema and chemosis produced by the fixative tend to push the treated area away from the eyeball while the tears effectively dilute the zinc chloride as it slowly penetrates the eyelid. The common basal-cell carcinoma of the lid margin may be removed with good cosmetic results because the eyelid soon pulls

up into normal position even though a considerable amount of tissue may have to be removed. Carcinomas of the inner canthal region, especially recurrent lesions, often extend posteriorly along the medial wall of the orbit for a considerable distance, but rarely is the eyeball involved; hence, this structure usually can be preserved.

#### OTHER EXTERNAL CANCERS

Carcinomas of the lips may be removed safely without the destruction of much normal tissue, consequently, the cosmetic results are excellent. Involved regional nodes are removed by surgical neck dissection.

Carcinoma of the parotid gland may be removed chemosurgically with good results, yet without damage to the facial nerve unless it is invaded by the neoplasm.

Carcinoma of the penis may be removed safely without amputation of the organ because, in most cases, the carcinomatous spread is not by continuous permeation through the lymphatics. However, the regional nodes may be involved owing to embolic spread through the lymphatics, and hence a groin dissection often is indicated.

Carcinoma of the vulva may be chemosurgically removed, even though the neoplasm spreads irregularly into the vagina and perineum and along the urethra. Involvement of the urethra requires the use of an indwelling catheter during the period of chemosurgical treatment.

#### THERAPEUTIC RESULTS

The microscopic guidance of excision makes possible an unprecedented degree of reliability in the treatment of the various forms of external cancer. Thus, the 5-year rate of cure in a consecutive series of 1554 cases of cutaneous cancer was 94%, which figure is well above any in the world literature for such a

series of cases. This record was attained, despite the fact that many of the lesions were extensive and over one-third had recurred after surgical or radiologic treatment. The series included 1071 basal-cell carcinomas (with a 5-year cure rate of 98.2%) and 483 cases of squamous-cell carcinoma (with a 5-year cure rate of 84.8%).

Squamous-cell carcinomas of the lower and upper lip also were treated chemosurgically with a 5-year rate of cure which was well above any in the world literature (326 cases of carcinoma of the lower and upper lips with a rate of cure of 91.7%). Similarly, in spite of the highly dangerous nature of carcinoma of the parotid gland and of malignant melanoma, the 5-year rates of cure were at the high levels of 54.5% and 40% respectively.

#### COMMENTS

The chief advantages of the chemosurgical method for the excision of cancer are its exceptional reliability and its conservatism. Both are the consequences of the microscopic control of excision which makes it possible accurately to follow out the clinically unpredictable extensions into the surrounding tissues. Sometimes these outgrowths follow specific structures; e.g., many infiltrative basal-cell carcinomas of the forehead and temples extend peripherally for considerable distances in the dermis. Other cancers may somewhat selectively follow facial planes, periosteum, perichondrium, embryologic fusion planes, nerve sheaths, lymphatic vessels or the adventitia of the blood vessels. Finally, some cancers exhibit irregular outgrowths even though there is no selective affinity for any particular tissue. The recognition of these silent extensions by means of microscopic visualization is a very important advantage of the method.

Other advantageous features of the method are the very low operative mortality rate (0.3%) and certain technical advantages that bring many previously inoperable lesions into the operable group.

Some degree of specialization in chemosurgery is necessary for best results, and a special clinic with facilities for making superior frozen sections is virtually indispensable. Eventually, a well-trained chemosurgeon operating in a well-equip-

ped and well-staffed clinic should be available in every large center of population.

#### CONCLUSION

The microscopic control afforded by the chemosurgical technic for the excision of external cancer is responsible for the unprecedented reliability and the conservatism attained with the method. The low operative mortality results from the lack of necessity for a general anesthetic.

### Multiple Sclerosis

Multiple sclerosis develops as an acute disease without warning in young adults and runs an intermittent course with exacerbations at intervals of weeks, months, or years, which last a few days to several months. In some cases complete disability results; in a few the process becomes arrested.

The triad of scanning speech, nystagmus, and intention tremors is of little value, because they occur in far-advanced disease, and may never occur. The early symptoms are extremely varied. Many patients are neurotic in the early stages, but recurrence of weakness or paresis in one or more extremities, diplopia, or unilateral blurred vision, vertigo, changes in emotional balance, a spastic or ataxic gait, or loss of bladder control and possibly nystagmus, pallor in the temporal half of the optic disk, loss of abdominal reflexes, or a Babinski sign should lead to the correct diagnosis.

The physician should maintain a challenging attitude toward this diagnosis. Once such a diagnosis has been made it is difficult for a physician seeing the patient for the first time at a later date to disavow the earlier diagnosis, because a changing clinical picture is characteristic of the disease. Although some warn against the use of spinal puncture,

pneumoencephalography, and myelography in these cases, most physicians who have a wide experience of the disease use these measures.

Most patients with this disease live many years. Myanesin and d-tubocurarine in oil have proved disappointing, and are neither safe nor dependable in treating muscular spasticity; adenosine is helpful in treating some patients with urinary incontinence. The aim of treatment is to mitigate the consequences of the disease. This is a task for the G.P., with the support of consultants. Exacerbations may be brought on by fatigue, emotional stress, trauma, infection, general anesthesia or extremes of temperature.

Frank discussion with the patient will prevent waste of time and money in a fruitless search for cure, and will help him to adjust to his disease. Much aid in meeting the problems of managing this disease may be obtained from the National Multiple Sclerosis Society, in the form of brochures for physicians and for patients in various stages of the disease. An attitude of cheerful enthusiasm on the part of the physician will be reflected in the patient's progress, and no physician should undertake to treat this disease with any other attitude.

Editorial, *J.A.M.A.*, 156:252, 1954

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## On the Therapeutic Uses of Citrus Bio-Flavonoids

*A non-toxic compound that includes vitamin P has widespread applications in the treatment of capillary fragility*

BORIS SOKOLOFF, M.D., *Lakeland, Florida*

MORTON S. BISKIND, M.D., *Westport, Connecticut*

WILLIAM CODA MARTIN, M.D., *New York, New York*

CLARENCE C. SAELOHOF, M.D., *Chicago, Illinois*

Some years ago, T. E. Boyd<sup>1</sup> pointed out that "there is a tendency to pay exclusive attention to the heart and the blood vessels," but that "it is in the capillaries that the essential business of the circulatory system is carried on." It is now realized that pathology of the capillary system is a contributing factor in many acute and chronic diseases.

### INCREASED CAPILLARY PERMEABILITY AND FRAGILITY

The capillary wall is a single layer

of endothelial cells bound together by cement, with millions of pores, which serve as "selective sieves" for plasma. It has been established<sup>2,3</sup> that this cement is susceptible to various chemicals. The normal capillary wall is impermeable to serum albumin and to serum globulin.<sup>4</sup> In certain disease conditions, these pores enlarge, permitting the passage of larger protein molecules. In later stages, the cement may be so weakened as to cause a rupture of the vessels.

In most bacterial and viral infections, there is a localized or gen-

From the Southern Bio-Research Laboratory, Florida Southern College, Lakeland, Florida.  
Aided by a grant from The Marcia Tucker Foundation, New York, N. Y.  
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eralized capillary syndrome of various degrees of gravity. Bacterial infections, as a rule, increase capillary permeability,<sup>5</sup> as do many chronic diseases of metabolic origin. All hypertensive diabetics of a large series<sup>6</sup> had an increase in capillary fragility; but this occurred in only 54% of nonhypertensive diabetics. Increased fragility was found in 80% of patients with rheumatic fever,<sup>7</sup> in 90% with spontaneous purpura; in the majority of cases of rheumatoid arthritis,<sup>8</sup> in 94% of allergic patients.<sup>9</sup> It has been indicated<sup>10</sup> that a renal capillary syndrome might be a factor in essential hypertension, and hypertensives often have increased capillary fragility.<sup>6</sup> Aschoff suggested that injury to the capillaries of the arterial walls might contribute to coronary thrombosis.

#### BIO-FLAVONOIDS: CAPILLARY PERMEABILITY FACTORS

Following the discovery of vitamin P, increasing evidence strongly indicated the beneficial effect of bio-flavonoids in hemorrhage which failed to respond to vitamin C, and several investigators<sup>11-14</sup> established this activity to be specific. Others,<sup>15,16</sup> in their turn, discovered that vitamin P has a specific affinity for the capillary cement and strengthens it when impaired. More recent work with a citrus bioflavonoid compound, known as CVP (citrus vitamin P), revealed its use-

fulness in many conditions of increased capillary fragility. CVP was administered with salutary effect in respiratory infections,<sup>17,18</sup> good results were reported in virus A influenza<sup>19</sup>; in radiation erythema<sup>20</sup>; in retinitis<sup>21</sup>; in bleeding duodenal ulcer and ulcerative colitis<sup>22</sup>; in bleeding cystitis<sup>23</sup>; in erythroblastosis<sup>24</sup>; in habitual abortion<sup>25</sup>; tuberculous hemoptysis<sup>26</sup>; in symptomatic hemorrhage and other hemorrhagic diatheses.<sup>27</sup> Others<sup>28</sup> found that CVP minimizes hemophilic bleeding. It was reported<sup>29</sup> that CVP decreased capillary fragility in elderly persons with many chronic ailments.

#### CITRUS BIO-FLAVONOID COMPLEX IN VIRAL AND BACTERIAL INFECTIONS\*

We may state that these compounds probably do not possess any direct *in vitro* antiviral or antimicrobial activity. Their activity appears to be mainly toward the control of the capillary syndrome induced by viruses and bacteria. This action appears to be anti-inflammatory. The bio-flavonoids markedly

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\*The preparation used in this study was C.V.P. A mixture of equal parts of whole water-soluble natural citrus flavonoid complex, and ascorbic acid. These citrus flavonoids, similar to, but not identical with, the original preparation of Szent-Gyorgyi, which he designated vitamin "P," have been described by Sokoloff, Eddy, and Reddy.<sup>16</sup> The commercial preparation, supplied by the U. S. Vitamin Corporation, contains in each capsule 100 mg. each of flavonoids and ascorbic acid. Except when otherwise specifically stated, dosage refers to the flavonoid component (100 mg. = 1 capsule).

shorten the period of some viral and bacterial infections.

Thus far, 125 cases of upper respiratory infections have been treated with CVP by the authors.

Following are some illustrative cases:

A woman, aged 49, with acute membranous tonsillitis and pharyngitis, t. 101°, was given 200 mg. flavonoids every 3 hours (1.8 gm. per day). In 48 hours, temperature was normal, infection and swelling gone, and the membrane peeled without bleeding off normal mucosa (after a total dosage in 48 hours of 3.2 gm.).

A woman, aged 55, was seen 48 hours after onset of a severe rhinitis. There was no fever, but a history of chest involvement following attacks of rhinitis, and subsequent asthma, which had required several hospitalizations 2 to 3 weeks; 200 mg. of CVP 3 times a day completely freed her of symptoms in 36 hrs. As she expressed it: "For the first time in my life the cold cleared up like magic."

A man, aged 42, with severe rhinitis, pharyngitis and tracheitis, temperature 101°; 36 hrs. after first dose of the flavonoid preparation, 200 mg. three times a day, the t. was normal and sore throat, cough and rhinitis had all disappeared; only some thickened mucus persisting.

Nine cases of virus influenza, serologically identified, were treated with CVP in relatively large doses.<sup>19</sup>

A typical example:

A white woman, aged 39, history of acute follicular tonsillitis with pharyngitis, onset abrupt, with chills, nasal discharge, hoarseness, t. 104°, persistent cough, muscular pain and general prostration complained of nose bleeds. The nasal mucosa was swollen, soft palate red. Pulse 120, no cardiac involvement. Urine—a trace of albumin, WBC 3600. Test positive for virus A in-

fluenza. Moderate tracheobronchitis. Treatment: CVP, 300 mg. every three hours for 48 hours. Total dose: 4.8 gm. Results: In 6 hrs. epistaxis arrested completely. 24 hours after starting treatment: profuse perspiration, temperature normal, nasal mucosa slightly swollen, discharge thickened; cough subsided to a considerable degree but remained for another 3 days.

In a small percentage of cases so treated, the improvement was moderate and the length of infection apparently only slightly altered. Yet even in these cases, a significant reduction in the inflammatory reaction appears to have taken place and there was less malaise and weakness than in previous attacks in the same patients.

Tested on a small series of cases of chickenpox, CVP reduced the eruption of macular vesicles and shortened the fever period to 36-48 hours.

#### MUMPS WITH SEVERE ORCHITIS

Two of us (W.C.M. and M.S.B.) investigated the effects of CVP in mumps with severe orchitis in a man of 43 (to be reported in detail elsewhere). This patient had a temperature of 104 F., unilateral parotitis, and severe unilateral orchitis, with swelling to more than twice normal size. Chills, intractable headache, nausea, vomiting and abdominal pain all contributed to severe prostration. On a dosage of 3 capsules of CVP every three hours day and night, and two intramuscular injections of ascorbic acid 1000 mg. at 24 hour intervals, temperature was reduced to 102 F. in 24 hours and to normal in 72 hours with subsidence of all symptoms except some remaining orchitis. Four days later the residual dual orchitis had almost subsided and this had disappeared completely in another week. Mumps of this severity in older males is usually

protracted, and there are often disabling and very persistent complications, none of which occurred in this case.

#### HEMORRHAGIC ULCERATIVE CYSTITIS

One of us<sup>23</sup> treated hemorrhagic ulcerative cystitis with CVP in a series of 19 cases; the results compared favorably with a series of cases treated with Gantrisin®. The following 2 cases are illustrative:

A white woman, aged 47, no children. Examined on May 24, 1954. Urine: Numerous RBC and pus cells. Culture showed: *Escherichia coli* and *Pseudomonas aeruginosa*. A pin-point ulcer near the r. ureteral orifice. Diagnosis: Hemorrhagic, ulcerative trigonitis and cystitis. Treatment: CVP, 2 capsules (200 mg.) at 8-12-4-8 started May 25. No local medication. May 27 tenesmus, frequency and urgency minimal; urine: several RBC. May 31 clinically well; urine occasional red blood cell, no pus cells; culture (48 hours) negative. No side effects. Total dosage of CVP 7.2 gm.

White woman, aged 42, two children. May 24, 1954: Urine—Many RBC and pus cells; culture *Escherichia coli* and *Pseudomonas aeruginosa*. Diagnosis: Hemorrhagic trigonitis and cystitis. Treatment: CVP, 2 capsules (200 mg.) at 8-12-4-8 started May 25. No other medication. May 27: Urine clear; a few RBC. Feels well. May 31: Urine no RBC or pus cells; culture (48 hours) negative. Clinically and bacteriologically cured. No side effects. Total dosage of CVP, 5.6 gm.

CVP compared with Gantrisin: With CVP, bleeding was arrested earlier, relief in 3-4 days as against 5-7 days with Gantrisin. The bacterial flora was normal in 5 days with either preparation. CVP has the advantage of providing physiologic medication without side effects of any kind. CVP induced no nausea

or gastric irritation, as did the sulfa in most of the cases so treated.

#### HEMORRHAGIC DUODENAL ULCER

Bleeding may occur at some time in 85% of cases of duodenal ulcer. The hopes for surgery in duodenal ulcer have been realized only partially. Opinion continues to shift between medical and surgical management, with the recent trend favoring medical treatment.

36 cases of uncomplicated, hemorrhagic duodenal ulcer were treated with CVP in cooperation with a group of gastroenterologists.<sup>22</sup> The results were satisfactory and, in all but two cases, bleeding was arrested in 24 to 36 hours.

A case which may be given as illustrative:

A white man, aged 62, executive. On October 1, 1951, he had his first intestinal hemorrhage, for which he had 4 transfusions and a diagnosis of duodenal ulcer. No history of pains or gastric distress. On February 12, 1953, he had a profuse bleeding from the nose and an intestinal hemorrhage. No transfusions, but was in hospital for a week. Present illness: On March 20, 1953 another intestinal hemorrhage—Hgb.—49%; RBC 2,140,000. Transfusion 500 cc. whole blood. March 23, continued to bleed. Transfusion 500 cc. whole blood. Started on CVP 2 capsules t.i.d., in the afternoon of March 23. In 24 hours the stools were lighter and in 48 hours hemorrhage was controlled. Patient had become again active in his business and was free of symptoms for 16 months. At this time, he began to take daily drinks of alcohol—another hemorrhage in October, 1954. This was controlled with CVP; he now takes CVP daily and no alcohol, and has had no further symptoms.

#### SYMPOMATIC HEMORRHAGE

In thrombocytopenic purpura

CVP produces certain palliation, reducing petechiae and bleeding. In non-thrombocytopenic hemorrhage, CVP is of definite therapeutic value. In most of the treated cases, CVP arrested bleeding whether from nose, hemorrhoids, or colon—in 24-48 hours.

The following case report is of interest as to the effect of CVP on bleeding in hypertension:

A woman, aged 56, referred to a Tumor Clinic for examination, complained of repeated severe bleeding from vagina, nose and gums. Hypertension of several years' duration. Examination revealed no malignant growth, heart, coagulation time, bleeding time all normal. Blood pressure: 205/110, weight: 225 lbs. Placed on CVP, 300 mg. daily, bleeding subsided and after 48 hours was minimal. By the third day it was completely arrested and there were no further episodes of bleeding during the next 6 months. The patient continued to take CVP.

It is in hypertensive patients that increased capillary fragility is of the greatest danger to health and to life.

#### TREATMENT OF CAPILLARY FRAGILITY

One of us<sup>29</sup> investigated the effect of CVP on capillary fragility in 16 cases, all older persons. Fragility was determined by the petechiometer and rechecked at 2-week intervals. The patients received 600 mg. of CVP daily. All had an increased capillary fragility. At the end of 4 weeks, all except 2 revealed normal capillary integrity. The observed response was all the more significant, as these patients were old and debilitated, all with some chronic disease and nutritional deficiency.

#### CVP IN RADIATION ERYTHEMA

When patients with cancer are submitted to deep radiation, the capillary system of the surrounding

healthy tissue is always injured. The erythema of the skin and mucosa is so caused. In an attempt to minimize radiation injury to the capillary system, one of us made a clinical investigation with CVP in co-operation with 37 radiotherapists over the country. Up to now, 1132 case histories have been collected and the report of the findings has been published elsewhere.<sup>30</sup> In most of these cases, the dose of CVP was 600 mg. daily, for 5 to 7 days prior to the initial exposure, and during the whole course of radiation therapy—altogether for 5 to 7 weeks. In the group of patients receiving CVP, there was marked increase in the tolerance to radiation as compared with the control cases. The radiation erythema was reduced considerably and general well-being of the patients was improved.

#### DISCUSSION

The integrity of the capillary system is an essential factor in health and disease. The capillary system may be injured by a multitude of agents. Many drugs, including antibiotics, chemicals and physical agents, bacterial toxins and viruses, nutritional defects, many metabolic disturbances e.g. diabetes, increase capillary fragility. Yet very little progress was made up to the last few years in the treatment of capillary fragility, and only quite recently has serious attention been paid to this problem. The work with bio-flavonoids provides effective means for controlling capillary injury, with widespread applications in the general practice of medicine.

#### SUMMARY

Increased capillary permeability and fragility are frequent phenomena in many disease conditions.

A citrus bio-flavonoid compound, CVP, highly effective in restoring capillary integrity to normal, was

30. Arons, I., et al: *Brit. J. Rad.*, 27:696-98, 1954.

administered with salutary effect in respiratory infections, hemorrhagic duodenal ulcer, hemorrhagic ulcerative cystitis, symptomatic hemorrhage, and radiation erythema. Promising effects were obtained in

mumps and chickenpox. It has only palliative effect in thrombocytopenic purpura and hemophilia.

CVP is non-toxic and can be administered in large doses without any ill effect.

### Management of the Third Stage of Labor

The vertex is delivered slowly and deliberately, the upper respiratory passages being aspirated immediately. The shoulders and body are slowly delivered, the body being delivered as far as the umbilicus, where the process is stopped and a loop of cord pulled down so that it may be palpated. The arrest in delivery at this juncture is for at least 3 minutes or until definite uterine contractions are palpated. The latter usually begin within 2 minutes. During the delay, further aspiration is carried out and the baby nearly always will cry spontaneously. This delay has the further advantage of giving the baby additional blood. The remainder of the baby is slowly delivered and the cord clamped and cut. Vaginal touch is immediately carried out to ascertain whether or not the placenta has separated. In most instances the placenta will be found separated and should be expressed according to the Brandt-Andrews technique which consists of upward stroking of the uterus and downward pressure on the separated placenta to complete its expression, the empty uterus being held out of the pelvis.

Pitocin 0.5 c.c. is given intravenously and ergonovine, 0.2 mg. in-

tramuscularly. The uterus is held high until it is fully contracted. The placenta is then carefully inspected. Cervical inspection is routinely carried out and perineal repair performed. A minimum period of 2 hours after the completion of the 3rd stage should be devoted to careful observation of the uterus and the general condition of the patient.

If the patient is delivered in the home, the following technique may be used: slow delivery of the baby; abdominal detection of placenta separation by noting the resumption of the globular form of the uterus and immediate application of the Brandt-Andrews expression.

The most unexciting stage of childbirth is the most frequent cause of material death. The 3rd stage of labor is still the most neglected phase. Postpartum hemorrhage occurs once in 60 deliveries or with sufficient frequency to alert everyone who does OB's to the necessity for improving his technique for conserving maternal blood.

Too frequently, we seek to save time by hurrying. It might be well to remember that if the mother can wait 9 months, we should be willing to wait 5 minutes.

Savage, J. E., *South M. J.*, April, 1953.

## Orbital Undercutting in the Treatment of Psychoneuroses, Depressions and Senile Emotional States

*Significant benefits have been obtained by this method of fractional lobotomy especially in depressions, anxiety and the senile emotional disturbances*

---

WILLIAM BEECHER SCOVILLE, M.D., *Hartford, Connecticut*

Five years ago the writer presented a new method of fractional lobotomy, permitting precise isolation under direct vision of various areas of frontal lobe cortex by means of cortical undercutting. The results, chiefly in schizophrenic patients, were summarized in 1950. Undercutting of the inferior or orbital surface of the frontal lobes has been carried out in 129 cases, and it was noted that when undercutting was limited to this area, no appreciable personality blunting or deficit occurred. This has recently been confirmed by the studies of Rylander and Sjoqvist. For this reason, selective cortical undercutting of the orbital surface of the frontal lobes has been done in

47 cases of the milder emotional and mental illnesses, including obsessive-compulsive neuroses, anxiety-tension states, somatic conversions, cyclic depressions, and senile emotional disturbances. The results have been gratifying in all categories, resulting in a lessening of anxiety and tension, a fading of morbid obsessive thinking, a lightening of mood, and relief from drug addiction, provided it is secondary to anxiety, pain or panic states. Fractional lobotomy should not be performed on constitutional alcoholic, psychopathic, or criminal types.

To our surprise, the senile emotional disturbances have shown the greatest benefit. In brief, it appears

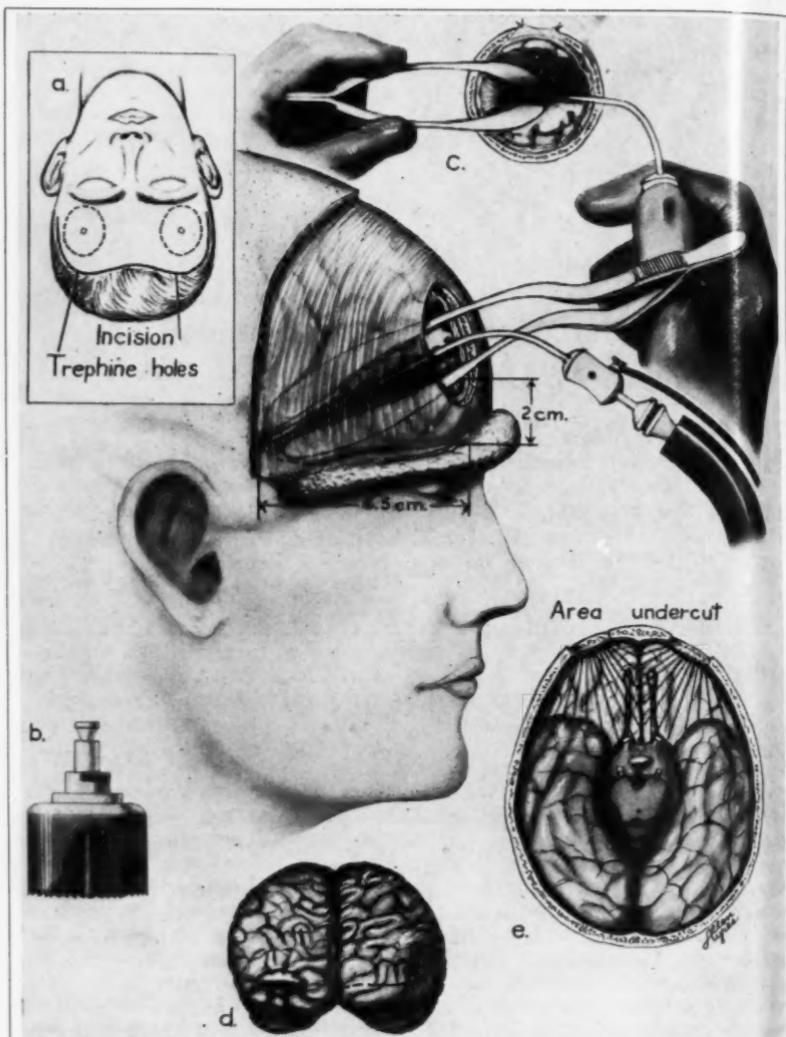


FIGURE 1  
PROFILE VIEW OF ORBITAL UNDERCUTTING OPERATION

- Location of Hairline Skin Incision and Trephine Openings.
- 1.5 Inch Trephine with Centering Pin.
- Line of Undercutting at Junction of Gray and White Matter Using Spatula Forceps and Fine Suction Tube.
- Location of Cortical Incision for Undercutting.
- Surface Area of Orbital Cortex Which is Undercut.

that the older the neurotic or depressed patient the more he will benefit by any form of lobotomy sufficiently limited to prevent personality deficit. In those agitated, sleepless and involutional cases thought to be incapacitated by the destructive processes of old age, deliberate destruction of an additional portion of the frontal lobe has restored them to a happy and frequently useful existence. This is a cause for surprise and surmise as to the deeper dynamics of senility. Seventeen patients over 65, 10 of them over 70 and 2 over 80 years of age, have been subjected to orbital undercutting with significant benefit and without appreciable deterioration.

#### BEST RESULTS IN DEPRESSIONS AND TENSION STATES

The degree of improvement in all categories has been in the following diminishing order: (a) Senile emo-

tional states; (b) depressions and affective illnesses; (c) obsessive-compulsive states; (d) psychosomatic conversion states including vague headache, tinnitus, pain and ulcerative colitis. Patients with severe organic pain are insufficiently benefited. There have been no adverse effects in the release of hostility or loss of social sensitivity, except for an uncovering of an underlying schizophrenia which occurred in 8 out of 47 cases. These have been aptly labeled pseudoneurotic schizophrenia by Hoch. Eventual benefit occurred to both the neurotic overlay and the psychosis, but relatives must be forewarned. There have been no infections; there was one death from coronary thrombosis; 5% had isolated convulsions permanently arrested by dilantin. In contradistinction to the standard lobotomy, improvement is insidious with no abrupt change in the overall personality.

#### True Hermaphroditism

An individual who has both ovarian and testicular tissue is a true hermaphrodite. Proof of the presence of both types of gonad in the same individual is histological, as the secondary sex characters may be affected by other factors, such as overactivity of the adrenal cortex.

Adopting these criteria, an examination of the literature has disclosed 59 unequivocal cases of true hermaphroditism, to which two further cases are added.

Two cases of true lateral hermaphroditism are reported and further progress of a third (bilateral) case is noted.

The first case presents the clinical problem of predicting the predominant psychological sex in adult life

when true hermaphroditism is diagnosed in infancy. In this case the chromosomal sex was male, which agreed with the preponderance of male gonadal tissue. On the other hand, the third case cited has grown up a psychologically normal male, but the chromosomal sex is female. This suggests that the chromosomal determination of sex is of limited value in these cases and must be considered in conjunction with all the available clinical evidence in deciding on the sex of upbringing.

The diagnosis of true hermaphroditism rests finally on the histology of the gonads, but a tentative diagnosis may be made on clinical grounds.

Bromwich, A. F., *Brit. M. J.* 4910:395-397, 1955.

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## Management of Urinary Tract Infections

*The advantages and disadvantages of many of the antibacterial agents and proper dosages of each is discussed in detail*

---

JAY P. SANFORD, 1st LT., MC, USAR\* and  
HENRY M. BALCH, MAJOR, MC, USAR\*

The basic and important lesion in chronic recurrent urinary tract infections is infection of the interstitial tissue of the kidney rather than the draining structures. The urinary tract's normal resistance to the development of infection is dependent in part upon the normal flow of urine. Failure to recognize and treat obstruction to drainage results in ultimate failure of specific antibacterial therapy. This point is well illustrated by the following case:

A 72-year-old man who had a slight asymptomatic enlargement of the median lobe of the prostate, following a right lower lobectomy for

carcinoma of the lung, was placed on continuous catheter drainage for 3 days, and developed a "cystitis" due to *Aerobacter aerogenes*. Residual urine in the bladder after voiding was only 30 to 50 ml. During a 6-months period, he was treated with sulfadiazine; sulfisoxazole (Gantrisin®); Mandelamine®, a triple-sulfonamide preparation; chlortetracycline (Aureomycin®); oxytetracycline, (Terramycin®); chloramphenicol (Chloromycetin®); and several experimental drugs, each with courses of two to four weeks. There was only occasional subjective improvement and no objective bacteriologic improvement during this interval. A perineal prostatectomy was then performed, following

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which his symptoms subsided, pyuria cleared and the urine became sterile.

Management of an episode of infection must include the detection and correction of obstruction as well as adequate systemic antibacterial therapy.

Gram-negative bacilli are isolated from 70% of "positive" cultures. These commonly include *Escherichia coli*, *Aerobacter aerogenes*, *proteus* species, *Pseudomonas aeruginosa*, *Alkaligenes faecalis* and *paracolon* bacilli. The more common gram-positive organisms encountered are *Micrococcus pyogenes* (staphylococci) and *Streptococcus faecalis* (enterococci). Almost any species of microorganism may be encountered.

#### BACTERIOLOGICAL EVALUATION

Antibacterial therapy should be based ideally upon bacteriological studies including antibiotic sensitivity determinations. However, in many instances, particularly with the first symptoms of infection, these studies may not be warranted or possible. Examination of the urine sediment, including a stained smear, will often enable rational empirical therapy to be instituted. Pyuria may be absent in a case of significant infection, particularly when caused by strains of *proteus*. Examination of a portion of the centrifuged sediment stained with methylene blue, Wright's stain, or Gram's stain is indicated.

An ordinary broth culture which is contaminated during collection may be very misleading. Some rely upon repeated cultures prior to initiation of therapy. More dependable is quantitative estimation of the number of bacteria present in a portion of urine. Mix 1.0 ml. urine with melted-agar medium, pour into a petri dish. After 24 hours of incubation, each bacterium will appear as a

separate colony which can be counted. On urine specimens obtained by catheterization, 1000 or more colonies per ml. are present in persons with urinary tract infections. Less than 1000 colonies per ml. of urine suggests contamination. The most common contaminants are *Staphylococcus albus* and *Alkaligenes faecalis*. Of more practical importance: if 2 to 5 bacteria were seen in each oil-immersion field upon examining the stained sediment of a fresh urine sample, 10,000 or more bacteria per ml. were present. If no bacteria are seen, the symptoms may well be due to nonbacterial irritation, rarely to tuberculosis.

A voided urine specimen from a male is usually satisfactory for study. In females, many catheter specimens, even under the best precautions, are contaminated. For initial evaluation of suspected infections, particularly if cultures are not to be done, the methods of quantitative study offer a means of avoiding catheterization in the female. The same precautions as used in catheterization are observed, then a voided specimen is obtained. The presence of 10,000 or more bacterial colonies per ml. of urine on culture, and/or 5 to 10 bacteria per oil-immersion field of the stained sediment, are strong evidence of bacterial infection.

#### DETERMINATION OF DOSAGE

Once the causative organism has been identified and, if possible, bacterial sensitivity studies done, adequate dosage of the appropriate drug must be given for an adequate period of time, the aim being to eradicate infection from the interstitial tissue of the kidney as well as other parts of the urinary tract. The common practice of using small doses of antibacterial agents may be acceptable only for prophylaxis, or in infection localized to the bladder (Table 1).

TABLE I  
RATIONAL APPROACH TO ANTIBACTERIAL THERAPY  
IN URINARY INFECTION<sup>1</sup>

Episodes of Infection	Diagnostic Methods	Bacteria Identified	Systemic Signs <sup>2</sup> of Infection	Suggested Therapy
1st	examination of stained sediment	cocci bacilli bacilli	0-4 0-2 2-4	penicillin sulfonamides tetracycline group or chloramphenicol
1st	culture and sensitivities (method of choice)	cocci or bacilli	0-4	based on sensi- tivity studies
2nd or more	culture and sensitivities (essential)	cocci or bacilli	0-4	based on sensi- tivity studies

1. Sanford, J. P., Favour, C. B., Harrison, J. H. & Mao, F. H., *Antibiotics Annual* 1954-1955. Medical Encyclopedia, Inc., New York, N. Y., pp 397.

2. Range of 0 to 4, the latter indicating severe sepsis.

From a series of urine cultures obtained from 358 individuals with clearcut evidence of infection, the species of bacteria found and the percentage of each judged to be "sensitive" to antibiotics are noted in Table 2. These cultures were obtained primarily from patients with chronic recurrent infections, hence the surprising portion of resistant strains. These findings are in contrast to the high proportion of "coliform" bacteria sensitive to streptomycin or the tetracyclines when these agents were first introduced. During the same period there has been no significant change in the proportion of bacterial strains resistant to the action of chloramphenicol. This emergence of resistance may be related, at least in part, to the widespread use of these drugs; while chloramphenicol, which today is often more effective, recently has had little general use.

The sulfonamides are still useful agents in urinary tract infections, especially those caused by *E. coli*. They are preferable in the initial treatment of infections caused by bacilli which have not been studied

by bacteriological techniques, unless the individual has signs of marked sepsis. As with sulfonamide therapy elsewhere, an attempt should be made to maintain a plasma level of 8-10 mg./100 ml. Likewise, sulfonamides find their place in prophylaxis following instrumentation and in situations when indwelling catheters are required. Sulfadiazine remains a satisfactory antibacterial agent. Newer agents, such as sulfisoxazole (Gantrisin<sup>®</sup>) and sulfadimetine (Elkosin<sup>®</sup>) are of equal antibacterial activity. These latter agents are more soluble and so are less apt to crystallize in the renal tubules. With all these agents adequate urinary output must be maintained. Recent reports suggest that the triple sulfonamide combination (sulfadiazine, sulfamethazine and sulfamerazine) may not show as great an antibacterial effect as the same quantity of a single sulfonamide though the advantage of increased solubility of the mixture remains.

Nitrofurantoin (Furadantin<sup>®</sup>) has a relatively broad antibacterial activity—against strains *E. coli*, *A. aerogenes*, *proteus*, *staphylococci* and

TABLE 2  
ANTIBIOTIC SENSITIVITY IN VITRO  
(Percent of Strains Sensitive to 32 mcg/ml or Less)

Bacterial Strain	no. of strains	chloramphenicol	streptomycin	chlortetracycline	oxytetracycline	tetracycline*	penicillin*
Proteus species .....	70	44	9	17	11	17	
E. coli .....	59	86	22	78	73	74	
A. aerogenes .....	104	59	8	34	32	37	
Pseudomonas species ..	28	21	18	57	61	67	
Misc. gram-negative ..	56	68	27	65	59	64	
Total: gram-negative ..	317	59	15	46	42	47	
Enterococci .....	53	49	—	45	36	49	21
Coagulase—staph. ....	26	42	—	46	31	47	23
Coagulase staph. ....	16	56	—	21	5	23	5
Total: gram-positive ..	95	48	—	42	30	44	19
Totals: .....	412	57	15	45	40	47	19

\*based upon only 316 strains included in larger group.

\*\*percent sensitive to 2 units/ml.

some strains of bacteria resistant to the usual antibiotics. The usual daily dosage is 7 to 9 mg./Kg. of body weight. Side effects have been noted in 14 to 25% of cases—usually nausea, occasionally vomiting.

Penicillin is still usually the choice in staphylococcal, group A streptococcal, and gonococcal infections. Although gram-negative bacilli are resistant to penicillin, if a high enough concentration is effected bacteria may be suppressed. It is often useful in combination with other agents; e.g., with streptomycin for enterococcal infections, or with chloramphenicol for severe proteus infections. As serious reactions appear to be on the increase, one should inquire as to previous penicillin reactions or allergic symptoms. If history is positive, a skin test with a dilute solution of penicillin should be done before administering the antibiotic. It is wise to inject the first dose into the triceps muscle of an arm, so that if signs of anaphylaxis appear, a tourniquet can be applied above the site of injection.

Apart from its use in tuberculosis, streptomycin should probably be reserved for specific situations based on sensitivity studies. Even with "sensitive" bacteria, urinary tract infections are apt to be persistent or recurring, so that bacterial resistance occurs readily.

The tetracycline series of compounds, chlortetracycline (Aureomycin®), oxytetracycline (Terramycin®), and tetracycline (Achromycin®, Panmycin®, Polycycline®, Steclin®, or Tetracyn®), are effective against most of the commonly isolated gram-negative bacilli with the exception of *Ps. aeruginosa* and *proteus* species. Tetracycline appears to be the least toxic of the group. However, symptoms of gastrointestinal dysfunction may appear with all these agents. Better results may be obtained using a mixture of equal portions chlortetracycline, oxytetracycline and chloramphenicol in the treatment of refractory urinary tract infections than with the individual drugs in comparable dosage.

Chloramphenicol (Chloromyce-

tin<sup>®</sup>) is effective against more strains of *A. areogenes* and *proteus* species than are the tetracyclines. There is very little intolerance. Although in a few susceptible persons aplastic anemia, leucopenia and thrombocytopenia may develop, only 29 of 1167 cases of blood dyscrasia recently reported had received chloramphenicol alone, and it is possible some of these may have been idiopathic anemias. The majority of these cases occurred in children. The risk is mainly from prolonged or repeated courses of the drug. If an individual has severe sepsis with urinary tract infection, chloramphenicol should be given, even in preference to the tetracyclines.

Polymyxin B (Aerosporin<sup>®</sup>) either alone or in combination with oxytetracycline is the drug of choice in infections due to *Ps. aeruginosa*. The parenteral dose should not exceed 2.5 mg./Kg./day. With oxytetracycline or tetracycline, it is synergistic. A total dose of 25 mg. intramuscularly per day of Polymyxin B, along with 1.5 to 2.0 gm. orally of oxytetracycline or tetracycline may be adequate for the eradication of *pseudomonas* infection.

Erythromycin (Ilotycin<sup>®</sup> or Erythrocin<sup>®</sup>) is reserved almost exclusively for penicillin-resistant staphylococcal infections. Depending upon specific sensitivity studies, it may be of value in enterococcal infections.

Although Bacitracin is nephrotoxic, in dosage below 100,000 units/24

hours with patient being watched carefully, its parenteral use is justified in urinary tract staphylococcal or enterococcal infections, in which other antibiotics have failed.

Certain antibiotics act synergistically in the control of a specific bacterium: e.g., enterococci—penicillin and streptomycin; *Pseudomonas aeruginosa*—oxytetracycline or tetracycline and polymyxin B; *proteus* species—chloramphenicol and penicillin. Here the use of a combination of antibiotics is highly desirable.

Optimal dosage of each antibacterial agent is difficult to define. If possible, one should obtain a blood level 5 to 10 times greater than the amount of antibiotic required to inhibit the growth of the instant organism in the laboratory. Generally, full systemic therapy will produce clinical improvement within several days. In order to insure sterilization of interstitial renal infection, therapy should be continued at least two weeks.

If either clinical or laboratory evidence of infection persists after a seemingly adequate course of therapy, or repeated episodes of infection occur, thorough reconsideration is essential. This should include bacteriologic evaluation, or re-evaluation, and appropriate urologic studies. For every patient at least an urinalysis, with examination of a stained smear of the sediment, should be done a month after apparent cure.

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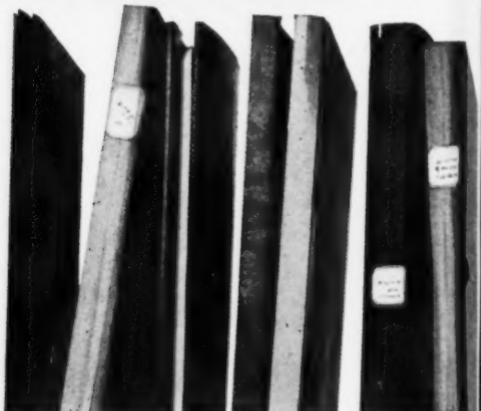
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*Early management of hand injuries which include instructions for treatment of fractures, nerve injuries and dislocations of bones*

DANIEL C. RIORDAN, M.D., *New Orleans, Louisiana*

Hand injuries lead the list of industrial accidents. The doctor giving the primary treatment has the greatest responsibility for the accurate diagnosis and proper management, the most important factors in determining whether the injured hand will be restored to usefulness.

### FIRST AID TREATMENT

The wound should be covered as soon as possible with a clean or sterile dressing. Probing of the wound should not be done. Antiseptics should not be applied to the wound. The hand should be splinted before transporting to hospital, if the damage has been severe.

The time, place, causative agent and mechanism of the injury should be determined. X-rays of the hand

should be taken, with the dressings in place, then the patient taken to an operating room, or an emergency room with complete operating facilities available.

### WOUND EXAMINATION

The examination should be made under sterile conditions, the examiner masked. The patient is not anesthetized. Sensation and active motion of all parts against resistance are tested. Tests are made for function of the profundi and sublimi of the fingers, as well as function of the intrinsic muscles of the fingers and thumb, and the wrist and finger extensors. If possible, the findings should be recorded at this time.

After the examination has been completed, the patient then may be

anesthetized. In many cases nerve blocks will suffice. General anesthesia is preferred in cases of extensive injuries. A bloodless field is produced by a pneumatic tourniquet, applied after elevation of the hand and arm, followed by complete expression of the blood from the extremity, by means of a rubber Martin bandage or Ace bandage, followed by the inflation of the pneumatic tourniquet.

The wound is then covered with sterile dressings and the surrounding skin shaved and cleansed with a soap or detergent and a suitable antiseptic, and the extremity draped so that the hand is freely movable. The surgeon then changes gown and gloves.

#### DEBRIDEMENT

If the wound has to be enlarged in order to properly examine and repair the damaged tissues, the principles laid down by Bunnell<sup>1</sup> should be adhered to. Incisions should parallel flexion creases; if a flexion crease has to be crossed, a zig-zag or curving incision is made to minimize subsequent scarring and contraction.

All tissues should be spared as much as possible. Any devitalized tissue should be excised. Only severely traumatized skin and traumatized, non-contracting muscle is excised. Tendons and nerves are preserved, unless all or parts of fingers are to be amputated. Bone fragments are preserved, unless they have been completely detached.

#### BONE INJURIES

X-rays should be carefully examined for dislocations of the various bones in the hand, which are common and easily missed. Bases of metacarpals may be dislocated and, unless recognized and corrected, will

lead to crippling deformity. The anterior half of the base of the metacarpal may be fractured and the shaft and base of the metacarpal dislocated dorsally. Open reduction is not usual, but internal fixation is frequently necessary. This is best obtained by use of Kirschner wires placed transversely into the adjacent normal metacarpal, or obliquely into the carpal bones to maintain the reduction. Three weeks' immobilization is usually adequate, occasionally 5, to prevent recurrence.

Dislocation of the metacarpophalangeal joint requires immediate reduction, usually by closed methods, but open reduction is required in some cases. The post-reduction immobilization should be in the position of flexion to allow torn ligaments to heal without undergoing shortening. After 3 weeks' immobilization motion should be started and carried out until a full range has been obtained.

Dislocation of the interphalangeal joints is a very common injury. Most of these can be reduced without anesthesia. After reduction test the joint for lateral stability. If the joint is stable, no immobilization is needed; if it is unstable, laterally, immobilize in a position of flexion for 7 to 10 days. Following this, motion is started. Early motion here is because of the tightness of fit of these joints to one another which will lead to a stiff joint if immobilization is prolonged.

#### FRACTURES

Metacarpal fractures near the base usually undergo shortening and rotation. If seen early, restoration of length and alignment is easily done by manipulation and can best be maintained by placing a Kirschner wire transversely into the adjacent stable metacarpal, or obliquely pinning the 25 fragments to the frac-

1. Bunnell, Sterling: *Surgery of the Hand*, J. B. Lippincott Co., 2d Edition, 1948.

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ture itself. If internal fixation is not used, it is usually necessary to maintain flexion of the metacarpophalangeal joint and the proximal interphalangeal joint, in conjunction with dorsiflexion of the wrist. Pulp traction is never to be used in injuries such as this; skeletal traction must be used if the fracture is to be treated by this method.

Fractures in the mid shaft or neck of the metacarpal usually result in angulation of the distal fragment with the metacarpal head prominent in the palm. These may be reduced by flexing the finger at the metacarpophalangeal joint and exerting pressure dorsally on the proximal phalanx, maintaining pressure on the proximal fragment at the same time. This position may be maintained by a well-padded plaster splint or cast. This type of treatment should not be used in elderly individuals, because of the danger of obtaining stiff joints from the position of acute flexion of all the joints involved. If reduction cannot be so maintained, internal fixation with a Kirschner wire or 2, placed obliquely across the fracture site or transversely into a stable adjacent metacarpal, is the treatment of choice. A minimum of 3 weeks' immobilization is usually necessary and if secure fixation with the Kirschner wires has been obtained, motion may be started at the end of this period.

#### REDUCTION OF PROXIMAL PHALANX FRACTURES

Fractures of the proximal phalanx frequently produce a dorsal angulation of the distal fragment as a result of the sling action of the extensor aponeurosis and the intrinsic muscles depressing the fragments, anteriorly, and tipping the distal fragment dorsally. Reduction of this fracture usually requires full flexion of the metacarpophalangeal joint

and partial flexion of the interphalangeal joint with pressure directed dorsally on the volar surface of the proximal phalanx. Occasionally, this type of fracture will be unstable and Kirschner wires placed obliquely across the fracture site are needed. Immobilization of this fracture should be maintained for 4 to 5 weeks, unless internal fixation has been used.

#### REDUCTION OF MIDDLE PHALANX FRACTURES

Fractures of the middle phalanx may have 2 types of deformity. If the fracture is proximal to the insertion of the sublimis tendon, then the distal fragment is brought into flexion by the sublimis tendon. The reduction is done by reversing the deformity and then flexing the metacarpophalangeal joint and proximal interphalangeal joint to release the pull of the sublimis tendon. If the fracture is distal to the insertion of the sublimis tendon, the proximal fragment is drawn into flexion and the distal fragment into extension. Reduction of this deformity is attained by reversing the deformity and flexing all joints of the finger. Usually, this fracture can be maintained in the reduced position by adequate splinting. A few cases require Kirschner wires placed obliquely, or longitudinally, to maintain reduction. These wires may be left in for 3 to 4 weeks. Motion is allowed after 4 to 6 weeks, if x-rays show evidence of healing.

Fractures of the terminal phalanx usually do not have serious displacement and require only immobilization. Union sometimes is slow and immobilization should be maintained until there is clinical and x-ray evidence of union before allowing active motion.

Fractures extending into the interphalangeal joint usually result in shortening and a lateral deformity.

All such fractures should be treated by continuous traction which is best done by skeletal means. Traction must be maintained with flexion at all joints and maintained until healing has occurred. Otherwise, the deformity will recur.

Avulsion of the extensor insertion of the distal phalanx of the finger is a very common injury. This results in the baseball or mallet finger and inability to extend the tip of the finger. Reduction is obtained by lessening the pull of the interossei and lumbricales. Relaxation of this extensor mechanism is obtained by flexing the metacarpophalangeal joint and proximal interphalangeal joint and hyperextending the distal interphalangeal joint. A small plaster splint and gauze bandage are applied without any padding between the plaster and the finger. The gauze bandage may be made to adhere to the skin by the use of tincture of benzoin or Ace adherent. If an x-ray check reduction is not perfect, open reduction is indicated. If the tendon has been avulsed without a bone fragment to indicate whether or not reduction has been obtained, an open repair of the tendon is indicated.

#### SERIOUS FRACTURED THUMB

Fractures of the thumb are generally treated in the manner outlined above, but the fracture-dislocation of the carpometacarpal joint of the thumb is a very serious injury. Anatomical replacement of the fragment is essential in order to prevent the development of traumatic arthritis and a painful hand. This can be reduced by closed means with a well-fitting plaster, maintaining pressure against the base of the metacarpal and skeletal traction in the longitudinal axis of the thumb. Pressure against the base of the first metacarpal must be maintained continuously. If x-rays show anatomical reduction cannot be obtained, op-

en reduction and internal fixation should be done, and maintained by Kirschner wires placed between the 2 bone fragments, or by drilling a hole through the 2 fragments, passing a wire through the hole and looping it around  $\frac{1}{2}$  of the circumference of the bone. After internal fixation, immobilization is maintained for 3 weeks, and if secure fixation was obtained at surgery, active motion may then be started.

#### TENDON INJURIES

Lacerations of hand tendons probably cause more deformity and limited usefulness than any other hand injury, primarily because so many doctors cannot resist the impulse to always repair a tendon laceration. From the flexion crease of the wrist, proximally, the flexor profundus and sublimis tendons may be individually sutured. From the flexion crease of the wrist to the distal flexion crease of the palm only the profundus tendon should be repaired. From the distal flexion crease of the palm to the middle phalanx of the finger, neither the profundus nor the sublimis should be repaired primarily. An accurate knowledge of the anatomy of the tendons is necessary for proper reattachment in cases of multiple tendon severances. From the distal flexion crease of the palm to the proximal interphalangeal joint level, the tendons should not be repaired primarily, simple suture of the wound, allow 4 to 6 weeks for complete healing and then apply a free flexor tendon graft. The sheath surrounding the tendon in this area fits the tendon and the bones so exactly that any swelling will result in complete adherence of the profundus and sublimis tendons, and a stiff finger. The best results are obtained when clean healing of the finger has occurred, followed by a free flexor tendon graft, expertly done, at a later date.

Extensor tendon lacerations may

be repaired at any level, primarily. If the laceration be underneath the dorsal carpal ligament, this structure should be excised and the tendon repaired. Usually, the tendons on the dorsal aspect of the wrist do not bow-string sufficiently to interfere with function, and removal of the ligament prevents the formation of adhesions to this structure. Repair of the extensor tendons is most difficult in the fingers, especially over the middle and distal joints. The tendon here is flat and thin and extreme care is required to get good approximation. The finest of sutures of the non-absorbable type should be used, or the pull-out wire technique. Immobilization is in a position of mild extension, for 3 weeks.

#### NERVE INJURIES

Generally, no attempt is made to repair lacerated nerves on the dorsum of the hand, since sensation here is not functionally important. Sensation on the flexor side of the fingers is of such importance that, whenever possible, the nerves should be repaired. A good result from an accurate nerve suture is usual. The same is true in lacerations of the sensory nerves in the palm, except for lacerations of the median and ulnar nerves. These two nerves, if properly identified, can be sutured successfully, as reported by both Bunnell and Boyes,<sup>2</sup> independently. A reasonably good return of function can be expected in this situation, since the motor branch at this level is pure and the fibers cannot be mixed up with sensory fibers.

Proximal to the transverse carpal ligament the nerves are mixed and there is no way to identify the sensory or motor components of the nerves. In case of laceration here, great care should be taken to try to

prevent torsion of the nerve, in the hope that sensory fibers will be approximated to sensory fibers and motor fibers to motor fibers. In the larger nerve trunks, small vessels may be visible on the nerve and serve as a useful landmark in making approximation.

Some recommend delayed, rather than primary, repair. Primary repair can be done satisfactorily in most cases, if the nerve has not been severely traumatized. Accurate anastomosis can usually be done, initially just as well as later. Late nerve suture is a little easier as fibrosis around the nerve has given a thicker nerve sheath. If the nerve has been severely traumatized, it is best to do a very simple suture to prevent retraction of the nerve ends, and to plan to do a secondary repair of the nerve 4 to 6 weeks later, after primary healing of the wound has been obtained.

#### SKIN CLOSURE

In wounds that have been incised or lacerated, simple closure of the skin edges is usually possible, best done by using stainless steel wire. The wire is without reaction in the tissues and the sutures may be left in for the full 3 weeks, or longer. No reaction results from the wire, a special advantage where perspiration occurs underneath the dressings. Wire gives good approximation of the skin, obviating the need for subcutaneous material, sometimes objectionable to the sensitive palmar skin.

Tendons, joints and nerves must not be left exposed. If a tissue defect is present and a simple flap can be swung over to cover the defect in a joint, tendon or nerve, this should be done. The donor area can then be split-grafted to give adequate closure. The blood supply of the flap is not to be devitalized, as a slough will make a larger wound defect. If

2. Boyes, Joseph H.: *J. Bone and Joint Surg.*, 32-A, 2:457, 1950.

tendons, nerves and joints can be covered with skin and subcutaneous tissue, the remaining defects can be covered by a split graft from forearm, abdomen or thigh.

In some cases, small flaps from an adjacent finger may be used to cover the defect, with subsequent skin grafting of the donor area. In many cases, however, the wounds are so extensive that abdominal flaps are necessary. Whatever the type of abdominal flap, absolute immobilization of the arm to the body is essential—best done with plaster.

#### POSTOPERATIVE SPLINTING

Whenever possible, the position of function should be assumed; the wrist is dorsiflexed, the finger joints all flexed to a minor degree, the thumb is partially adducted and opposite the index finger on its flexor surface. This position of function may be used for the postoperative dressing of most tendon injuries in the fingers or palm or for nerve injuries. If the extensor tendons have been damaged, the fingers will have to be extended to a greater degree, but *never* in complete extension. The fingers should be separated with gauze and, if there had been extensive damage, a pressure dressing of mechanic's waste or cotton should be used. The dressing itself is made stable by the application of plaster.

Continuous elevation of the hand should be maintained for 36 to 48 hours. Antibiotics are given, the choice depending upon the condition of the injury and the probable nature of the contaminating organism. Tetanus antitoxin should be administered, or the toxoid, if prior inoculation has been given. If there is no clinical evidence of infection within 48 hours, the patient may be allowed to be ambulatory and continuous elevation of the hand discontinued.

If tendons and nerves have been

lacerated and repaired, 3 or 4 weeks of immobilization is necessary. Then a graded exercise program, full strength should not be allowed for at least 6 weeks. If motor nerves have been severed, corrective splinting should follow the removal of the postoperative dressing. In the case of the ulnar nerve, this splinting should be directed towards getting hyperextension of the metacarpophalangeal joints; in median nerve injuries, toward holding the thumb in the partially or fully opposed position. Frequent visits and instruction as to the proper type and amount of exercise should be given. If available, the patient may be turned over to a physical therapist, under the doctor's supervision.

If fractures are present and have been treated, immobilization will have to be continued for a longer period. Adjacent uninjured parts may be allowed motion as soon as possible so that the entire hand will not become stiffened through disuse. If fractures have been internally fixed with Kirschner wires and secure fixation has been obtained, motion may be allowed at the end of 3 or 4 weeks.

#### SUMMARY

The principles of early management of hand injuries are:

1. First-aid dressings and splinting as soon as possible; sterile if available.
2. X-rays of all hand injuries, done without disturbing the dressing on the hand.
3. Examination of the hand under sterile conditions, preferably in the operating room, done with the patient's full cooperation. Accurate determination of motor and sensory damage should be made at this time.
4. Surgical repair of the damaged hand should be done in an operating room or emergency room

with complete operating facilities available. Office procedures are condemned.

5. Primary reduction of fractures and dislocations should be done, using internal fixation by means of Kirschner wires, if necessary.
6. Lacerations of flexor tendons should be repaired by the "2, 1 or none" law. Nerves should be primarily repaired, if possible.
7. Primary skin closure should be done. Split-skin grafts may be used if tendons, nerves and joints will not be left uncovered. Local flaps or abdominal flaps may be used if tendons, nerves or joints will be left uncovered.
8. Postoperative dressings should splint the hand in the position of function whenever possible. Pressure dressings should be used to prevent unnecessary edema. Elevation of the hand immediately postoperative and for 48 hours should be carried out in most hand injuries.
9. Postoperative immobilization should be continued for 3 weeks, this followed by a graded program of exercises to restore motion, unless fractures are present; fractures demand a longer period of immobilization.

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## Idiopathic Pruritis—New Etiology and New Specific Therapy

*A combination of amino acids, from which excess methionine has been removed, shows promising results in the treatment of pruritus ani*

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Pruritis, or itching, is a symptom, designated according to anatomical location (pruritus ani, pruritus vulvae); according to etiology (psychogenic, hormonal or menopausal, parasitic, fungous, allergenic, following use of antibiotics); and as a complication of certain pathologic states (cryptitis, proctitis, hemorrhoids). One group, its cause remaining unknown, is designated as idiopathic or essential pruritis.

Most will agree that the treatment is generally unsatisfactory. Robinson<sup>1</sup> has stressed that the fundamental problem in pruritus ani therapy has been the recurrence of symptoms when local medication is stopped. Turell,<sup>2</sup> after studying the

effect of corticotropin and cortisone in anogenital pruritis, concluded that proctologic lesions with anal pruritis should be removed surgically. Before starting on treatment of pruritis, the doctor must investigate the direct and underlying causes. Factors responsible may be hormonal, psychogenic, fungous, parasitic, bacterial, allergenic, chemical, unhygienic, and systemic changes incident to pregnancy or diabetes.

Pruritus ani may be caused by local irritants, local disease conditions, intestinal parasites, endocrine imbalance, allergens, and certain antibiotics. In most patients the cause is not readily detected and the pruritis is, at least temporarily, classified as idiopathic or essential.

Bodkin and Ferguson,<sup>3</sup> in a long-

1. Robinson, H. M. & R. C. V., *J.A.M.A.*, 155:1213.  
2. Turell, R., *J.A.M.A.*, 152:808, 1953.

term clinical investigation, found that in many patients with idiopathic pruritus ani, an irritant escaped from the anal canal and set off the itching — scratching — infection cycle. Chemical studies revealed:

"Attempts at imitating the action of pruritus on healthy skin led to the use of an agent known as ammonium oleate. This causes actual pruritus in some cases. In addition, . . . the irritant forming the whitish edges of skin along the fissures may be reproduced at the same time by an astringent agent such as tannic acid. Another series of compounds inducing irritation similar to pruritus is the ammonia series. Dilute solution of ammonia water reproduces many of the itch symptoms. Finally, the general condition of poor nutrition in the area of pruritus ani may be reproduced by an ointment containing large amounts of microscopic crystalline methionine (an amino acid.) . . ."

"It is entirely possible that the excretion leaking from the anus and the excessive amount of sweat found in the perineal area combine to cause pruritus ani, whenever the nutrition of the skin is so changed, to allow the result."

This discovery of an irritant escaping through the anus of patients with pruritus ani, and the experimental production of pruritus ani in healthy skin by the application of astringents, direct irritants, or protein precipitants, has virtually abolished the classification of idiopathic pruritus ani.

In vitro studies<sup>4</sup> revealed that these etiologic irritants are most effectively rendered inactive by buffered protein or amino acid solution. An amino acid and polypeptid mixture derived from lactalbumin hydrolysate was studied but certain

acids were found to be irritating: "Separate applications were made of the amino acids listed below.

Amino Acid	Effect
Arginine	Indifferent
Histidine	Slight irritation
Lysine	Indifferent
Tyrosine	Indifferent
Tryptophane	Slightly beneficial
Phenylalanine	Slightly beneficial
Cystine	Slightly irritating
Methionine	Strongly irritating
Threonine	Indifferent
Leucine	Slightly beneficial
Isoleucine	Indifferent
Valine	Slightly beneficial"

The discovery that certain of the amino acids in the combination caused irritation led to the formation of a novel complex from which significant amounts of methionine, cystine and histidine, together with certain water-insoluble compounds, have been removed.

One hundred patients suffering from intractable pruritus ani were treated with an ointment\* in which 10% lactalbumin hydrolysate containing specific therapeutically effective amino acids, was incorporated in a polyethylene glycol 1500 base. Potential irritants such as methionine and cystine were removed and isotonicity was maintained to eliminate the danger of irritation or other side-effects.

In this series of 100 patients Bodkin<sup>6</sup> made the following observations:

"The skin changes which take place while healing are easily observable and are both interesting and significant. The moisture disappears first. This is followed by fading of redness in inflamed areas. The white ridges where precipitation of protein has been pronounced become less noticeable, until finally the perianal re-

3. Bodkin, L. G., *Am. J. Dig. Dis.* 18:59-60, 1951.  
4. *Ibid*

\*Hydrolamins Ointment®, Lewal Pharmacal Co., Chicago

5. *Ibid*  
6. *Ibid*

gion assumes its normal color. The fibrotic, inelastic skin which fuses readily becomes soft and pliable. Within a few weeks' time there is every appearance of normal skin.

" . . . Salve was applied in every case to the perineal area and if necessary around the vaginal or scrotal areas as well. Most patients reported immediate cooling effect from the salve. This effect lasted for approximately 24 hours.

" . . . Relief was experienced im-

mediately in 98 cases . . . The average time is 19.5 days. In the group there were 10 cases which had only partial relief and 2 cases with no relief. This represents a percentage of 88% complete success.

" . . . This mixture of amino acids is a specially treated combination from which excess methionine has been removed. This mixture . . . when applied to areas of pruritus, has shown effectiveness far greater than previous expectations in the treatment of pruritus ani."

## Hypertension and Coronary Occlusion

Existing concepts concerning the relationship of hypertension to coronary occlusion are in need of revision when applied to the age groups of 60 years and older. Readings hitherto considered abnormal can no longer be taken as valid, for "high" systolic and diastolic blood pressures have been found in a majority of individuals of these age groups. New definitions of hypertension based on the age and sex of the patients are evidently necessary. The average blood pressure rises with age and varies with sex, and is therefore not covered by a single definition of hypertension for all ages. In order to define anew the relationship existing between hypertension and coronary occlusion, the author studied 600 consecutive patients with such occlusion, as seen in private practice. The group studied included 500 men and 100 women. Patients older than 64 years were not included because the criteria for blood pressure limits existing beyond this age had not yet been established. The blood pressure which preceded the coronary occlusion was taken as the criterion for the conclusions drawn with respect to the group of patients here reported.

It was found that men sustain coronary occlusion much more frequently than women, and at an earlier age. The frequency of hypertension in the men averaged 27.2%, and increased at an earlier age. More than 70% had had normal blood pressure before the onset of the coronary occlusion. Hypertension, therefore, is not the all-important factor in the causation of coronary occlusion in men. This occlusion differs from that hitherto held. With respect to the women patients, 71% had had hypertension preceding the attack. In women who suffer an attack of coronary occlusion hypertension is therefore a significant etiologic factor. A post-mortem study recently made by the author confirmed his clinical findings: hypertension did not appear to be a factor in producing coronary disease and occlusion among men, but was a definite factor in its causation among men. Also briefly discussed are the possible effects of serum cholesterol, of the S<sub>f</sub> 12-2 lipoprotein fraction, and of the sex hormones on atherosclerosis and hypertension. It is concluded that these fields of investigation hold great promise for the treatment and prevention of coronary disease in men, and of hypertension in women.

Master, A. M., *Circulation*, 8:170, 1953.



## Allergy in General Practice

*The general practitioner should have the ability to recognize causes of allergic diseases and a knowledge of the therapy required*

J. P. SANDERS, M.D., Shreveport, Louisiana

To differentiate allergy from similar diseases, thorough examination and painstaking family and patient history are essential. The over-all care of the patient is the job of the family doctor. The home should be free of dust or other allergens to which the patient might be sensitive. If the patient has symptoms while he is at his office or his place of business, then it is usually the G.P. who has to survey that place of work and determine what factors are causing the symptoms. He may have to decide where the patient must travel, what foods and what pollens to avoid. The patient should not be advised to "move to a higher and drier climate."

Materials for desensitizing the patient to any allergen may be danger-

ous. The G.P. will frequently be called upon to administer the extracts the allergist has prescribed. Antihistamines alone with desensitizing extracts make possible much larger doses of the allergen and thereby hasten the desensitizing process.

The special educational training of the patient is probably the most important of the whole allergic regimen. The patient has to be told that any treatment will have to be carried out over a long period of time.

Many allergic patients are sensitive to many allergens, a few of which are causing his trouble.

The patch test is one of the commonest. A bit of material placed on a piece of sterile gauze, moistened to adhere, is attached to healthy

skin for 24 to 48 hours; can be repeated without danger or difficulty.

In all cases of allergy there is risk of throwing the patient into an attack; have adrenalin ready.

Block testing has one advantage. If one block of 7 substances is negative, it is not necessary to test the patient for the other six.

If symptoms occur only in the spring, we think of pollination of flowers, grasses, trees, etc., as being the offenders. Hayfever in autumn--think of ragweed or one of the fall grasses. Constant symptoms are usually due to foods or surroundings. One sensitive to house dust will usually have his symptoms when exposed to dust in office, automobile, or any other place.

Does the condition incapacitate, or is it only a nuisance? Women sensitive to cosmetics may find it difficult to attend religious or social gatherings.

The value of the antihistamine varies with the type of allergy, the length of time of the disease, and many other factors. The eczemas are the hardest of the allergies to treat.

Asthma and hayfever usually respond to antihistamines.

Combinations of these are sometimes of more value than either one alone. Ephedrine with amyntal is a favorite. Adrenalin in a 1/1000 solution, adrenalin in oil (hypo) and adrenaline in glucose, 1/1,000,000 solution (IV) are very effective in asthma, hayfever and some of the dermatoses. Infusions of ephedrine, histadyl and other antihistamines may give happy results.

When a child comes with a severe case of asthma or rash, and has responded to no other treatment, ACTH or cortisone will relieve quickly and give opportunity to further study. For a secondary invader, the addition of antibiotics is indicated.

The G.P. and the specialist in allergy must work as a team if the patient is to get the best medical care. The G.P. must keep himself informed on allergic diseases, be on the lookout for them, and take chief part in the care of the patients afflicted by them.

*J. Louisiana State Med. Soc., 107:142-147, 1955.*

### **Treatment in Acute Hematogenous Osteomyelitis**

This is primarily a blood-stream infection occurring in children. The incidence has decreased markedly in recent years because of the great improvement in general therapy and the development of antibiotics. Most commonly caused by *Staph. aureua*, the bacteria are filtered out of the blood stream to the metaphyses of the long bones.

Treatment consists of penicillin IM every 3 hours until the clinical signs have disappeared and the infection is under control, 3,000,000 units over a period of 21 days. If the organism is resistant to penicillin, other antibiotics are substituted depending on the sensitivity tests.

Treatment is supplemented with

blood transfusions, maintenance of the water, electrolyte and protein balance, etc. Immobilization in plaster will help arrest the infection, minimize the absorption of toxins, and avoid the possibility of a pathologic fracture.

The mortality rate has been greatly reduced by withholding operative drainage of the bone lesion in the acute stage. Surgery should be delayed until the autogenous protective mechanism and barrier have been set up, and the bacteremia has cleared.

Small abscesses may be treated by repeated aspiration and penicillin instillation of the cavity.

*Kaye, B. D., J. Maine M. A., 45:269, 1954.*

## Radioisotopes in Medicine

*An analysis of the components and experimental usage in treatment and diagnosis by this new substitute for radium*

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A discussion of radioisotopes requires a definition of terms, so that doctors generally may understand the meaning of some of the phraseology of the radiologist and physicist.

There has been increasing interest in the use of radioisotopes in medicine since 1934 when radioactive sodium was first reported by Fermi. The increasing availability of radioactive elements from the Atomic Energy Commission has made their usefulness widespread for both clinical and investigative uses. Clinical use of isotopes is still limited to a small number of compounds, but their utilization as tracer substances in medicine will certainly be many times multiplied.

*In general, isotopes are 2 or more*

chemical elements which have the same atomic number, the same nuclear charge, the same number and arrangement of orbital electrons and identical chemical properties, but which differ in atomic weight or nuclear structure. These are stable compounds. Radioactive isotopes are unstable, and, in addition, have radioactive properties; i.e., they undergo nuclear disintegration with loss of radiant energy in the form of A, B, and G rays, and the resultant product is a stable element of lower atomic weight. Such substances occur in nature as uranium and thorium and their daughter compounds, the best known of which are the uranium decay products, radon and radium.

The half-life of a radioactive com-

pound or element is that time in which  $\frac{1}{2}$  the atoms of the compound or element undergo degeneration with an accompanying release of energy; e.g., if we have 1,000 atoms of radioiodine ( $I^{131}$ ), which has a half-life of 8 days, at the end of that time, there will remain 500 atoms. 8 days later, 250 atoms will remain, and 8 days later, 125, and so on. This process is spontaneous; the rate varies with each isotope and is constant for each.

These materials' amounts are defined in terms of radioactivity. The standard unit is the *Curie*, the emanation of one gram of radium. In practice, we deal with the *millicurie* and *microcurie*. Only 3 of these isotopes are discussed in detail:

1. Radiophosphorus ( $P^{32}$ ), with a half life of 14.3 days, is produced chiefly in the atomic pile, and emanates Beta rays only. It is administered either orally as sodium phosphate or intravenously as sodium acid phosphate.

$P^{32}$  has produced favorable results in chronic myelogenous and lymphatic leukemias, benign follicular lymphoma, polycythemia vera rubra, and in 20% of the cases of Hodgkin's disease.

2. Radioiodine ( $I^{131}$ ), has a half life of 8.0 days; is produced chiefly in the atomic pile, and emits both B and G radiation. B has an average tissue penetration of 2.2 mm, thus confining locally. G rays being more penetrating, make it possible to measure the amount of radioactivity of  $I^{131}$  either *in vivo* or *in vitro* by means of a geiger counter. The isotope is administered orally as sodium iodide.

#### THYROID ACTIVITY

Among the better known uses of  $I^{131}$  have been studies of the function of the thyroid gland and treatment of hyperthyroid and malignant states. These studies are much more

accurate in determining the activity of the thyroid than the BMR and there has been found to be little correlation between the two.

A calculated dose is given to the patient by mouth, 24 hours later the amount of radioactivity in the thyroid gland is determined by means of a geiger tube and a counting device. From a simple mathematical formula, the % of iodine absorbed by the thyroid can easily be calculated. We must be certain that the patient is on a low-iodine regimen — off of Lugol's, thiocyanates, and soluble sulfa compounds — for 1-4 weeks prior to uptake studies. Diagnostic x-ray studies may alter the  $I^{131}$  uptake for periods of from 10 days to life.

Very promising results in the treatment of hyperthyroidism have been obtained using small doses of  $I^{131}$ , repeated 1 or 2 times as indicated. In some clinics, it is felt that all cases of true Graves' disease, adequately treated, will respond. Of the failures reported, a high percentage can be attributed to failure to repeat the treatment as needed. Care must be exerted, of course, to avoid myxedema.

Results have been encouraging in many cases of true angina.

#### BRAIN TUMORS

In the detection of brain tumors  $I^{131}$  is tagged to di-iodofluorescein, which has a special affinity for brain tissue, especially that which is highly vascular and undergoing mitotic development. Following the injection of the radioactive compound opposing sites over the skull are studied with a geiger tube and counter, and the difference in radioactivity over the compared areas serves as a key to the underlying vascular and cellular activity. By this method many intracranial growths can be readily outlined by careful study.

3. Radiogold (Au<sup>198</sup>), with a half-life of 2.7 days, is produced in the atomic pile, is both a B and G emitter, and is administered in colloidal suspension by injection. It has proven useful in the infiltration of carcinomatous masses which are otherwise inoperable or which cannot be adequately treated by surgery or by x-ray because of the condition of the overlying skin, the site of involvement, or adjacent structures which are involved. Success has been reported in the treatment of cancer of the prostate which has broken out of the capsule but which has not undergone distant metastasis. Rather spectacular results have been seen in the control of pleural

and peritoneal effusions of malignant-tumor origin, offering the patient a more comfortable existence with infrequent tapping, as a result of control of the peritoneal and pleural metastasis.

A great deal of work has been done in other diseases and biological studies, using these and many other isotopes. Radiocobalt (Co<sup>60</sup>), also pile-produced, is a strong gamma source. The half-life of 5.3 years has made this element an important substitute for radium and it is often referred to as the "poor man's radium."

*The Recorder (Columbia S.C. Medical Society) May, 1954.*

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## Human Nutrition and the Sophistication of Foods and Feeding

*Some new concepts on the advantages obtained by the infant from human milk and the detrimental effect of cows' milk*

---

B. S. PLATT, M.D., *London, England*

Until quite recently there has been no convincing evidence for the superiority of human milk to cows' milk in the feeding of human infants. Such differences as calcium content 5 to 6 times greater in cows' milk than in human milk have been overlooked. After 6 to 10-months' feeding on cows' milk the proportion of calcium in the infant's body is more than half as much again as that in the infant fed on human milk.

It has been stated that hypercalcemia must be quite a common disorder. The frequency with which a history of feeding on cows' milk is reported suggests that the practice is an important factor in the causation of the condition. It may be wondered whether we should regard

the mother during lactation, as not merely a provider of food, but also as a supplier of substances ready made for use by the infant until such time as he can synthesize them for himself.

Milk sugar is made up of glucose and galactose; galactose is found in the cerebrosides of the central nervous system and in mucopolysaccharides in connective tissue. We do not know if galactose can be synthesized in any human tissue at any age, except in the mammary gland. Galactose may be a substance for which the human infant is dependent on his food—that is, in this case it would be an "essential" nutrient in the sense that some amino acids and the accessory food factors are "es-

sential."

#### MYELINATION

The cerebrosides are the principal lipids of myelin, most of which is laid down after birth. Myelination continues until perhaps the 5th to 6th year of life, and the progress of myelination of nerves may well be determined by the activity of the muscles with which they are connected. An infant fed on cows' milk stores nitrogen at a much greater rate than does one on breast milk, and at 6 months the percentage of nitrogen in the body of an infant fed on cows' milk is twice that in the body of one fed on human milk. Presumably most of this N is stored as muscle protein, and we may infer that in the infant fed on cows' milk the rate of muscle development will be more rapid than in the breast-fed infant. If this also entails more rapid myelination of the appropriate nerves, and if the galactose for the synthesis of myelin must come ready synthesized from the food, we have

to take account of the fact that the cows' milk-fed baby gets only two-thirds of the amount of lactose which he would receive if he were being fed the corresponding amount of human milk.

#### COLLAGEN DISEASE

A group of disorders of connective or mesenchymal tissue have been called "collagen diseases." Quite a lot of evidence has been adduced that the mechanisms of formation of abnormal glycoprotein are associated with the morphogenesis of these diseases. Here it is suggested that the supply of galactose—or substitution of glucose for this sugar—in the feeding of the infant and young child may be a factor in the occurrence of a number of diseases which might be identified with the sophistication of living. A plea is made for a study of the effects of changes in feeding habits consequent on the various methods of sophistication of foods.

*Brit. M. J.* 4907:179-184, 1955.

#### Pyridostigmin (Mestinon®) in the Treatment of Myasthenia Gravis

In 1935 the injection of neostigmine was shown to provide a rapid and specific diagnostic test. As a result hundreds of new cases were identified. A year later it was reported that patients could be maintained on tablets of neostigmine given by mouth, and the successful treatment of myasthenia gravis began.

For 18 years neostigmine has been the mainstay of therapy in restoring hopeless invalids, unable to swallow food, to nearly normal activity. In parenteral form it has tided patients over crisis or through major surgical procedures, making it possible,

by thymectomy, in selected cases, to obtain complete and permanent remission.

An analogue of neostigmine, *pyridostigmin*, is an effective antimyasthenic compound when 60 mg. is used for each 15 mg. of neostigmine. It is free of disagreeable gastrointestinal effects, but in some cases is not as effective as neostigmine. In those who cannot tolerate neostigmine without atropine, pyridostigmin is superior to neostigmine. There is danger of masking overdosage with neostigmine when atropine is taken.

R. S. Schwab, et al, *The New England J. Med.* 251:271, (Aug. 12), 1954.

## Estrogens and Acne

*Two preparations, a cream and a lotion, brought remission from severe chronic acne in a large majority of the cases tested*

IRVING SHAPIRO, M.D., Newark, New Jersey

In treating severe chronic acne two preparations were used: (1) 2.5 mg. per gm. water-soluble estrogenic substance equine (Premarin Cream® Ayerst) in a vanishing cream base; (2) 1 mg. per cc. estrogenic substance in 70% alcohol (Premarin Lotion® Ayerst).

A cotton applicator was used to apply the lotion twice a day for 4 to 6 weeks, average daily 1 or 2 cc. lotion or 1 to 2 gm. cream. This amount would be enough to treat an area 6 to 8 inches square. When the skin became less oily only one bedtime application was used. Stubborn patches received extra attention. No other treatment was given; no diet followed.

Cases chosen were over 5-years' duration, severe scarring types

which had relapsed after x-ray, vaccine, diet and other therapy.

In 80% of chronic severe acne cases a remission was produced using topical Premarin in 70% alcohol twice daily for 6 weeks, then sharply reduce dosage lest systemic effects be produced. Stubborn areas require more persistent attention. Only 5% of these cases required a stronger, and another 5% a weaker, concentration to produce initial results.

Once oiliness is sharply reduced the dose is tapered rapidly and a small maintenance dose is kept up for 6 to 8 weeks more. With individualized dosage no systemic changes, such as menses change, altered libido, nausea, gynecomastia need be produced. A 1:25 milligram-per-

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gm. Premarin Cream is excellent for maintenance.

Relapses occur in 10% of the cases, are mild, and easily brought un-

der control with another short course of topical estrogens.

*J. Med. Soc. New Jersey*, 52:6-8, 1955.

### Management of the Tuberculous Patient

Treatment should be delayed until proof of active tuberculosis is obtained. Suggestive x-ray shadows are not sufficient. A substantial percentage of patients with shadows typical for tuberculosis are suffering from a different disease. The assignment of such patients to a sanatorium may constitute a grave injustice. The situation is even more serious if antibacterial drugs which render bacteriologic confirmation difficult have been given.

The presence of T.B. in pulmonary secretions indicates active and potentially progressive pulmonary tuberculosis. Methods of demonstrating T.B. are much more sensitive now but require more skill and judgment than is available in many excellent clinical laboratories. Falsey positive findings are serious to the patient.

Three to 6 months of bed rest with bathroom privileges, followed by a similar period of slowly increasing activity, often suffice for minimal disease when full use is made of more direct, modern measures.

All patients with active T.B. should receive treatment with antibacterial drugs, continued throughout the period of activity and for at least 6 to 12 months after.

Streptomycin, although never used without auxiliary drugs, remains a dependable remedy, 1 gm. IM 2 or 3 times each week usually stops the multiplication of T.B. Pa-

tients who are severely ill may benefit by daily doses for 4 to 8 weeks or until evidences of disease diminish.

Isoniazid possesses a degree of anti-tuberculosis activity comparable to that of streptomycin. It is rarely used alone because of rapid appearance of drug-resistant organisms, but in combination with streptomycin, 100 mg., 2 or 3 i.d., is well tolerated by most persons. Recently peripheral neuritis has been reported in considerable numbers. It is uncertain whether vitamin preparations are effective in either prevention or treatment of isoniazid neuritis.

One of the virtues of isoniazid is its diffusibility through the body and into the interior of cells.

Para-aminosalicylic acid (PAS) as companion drug to streptomycin is steadily losing ground to isoniazid.

Viomycin has become established as an effective and safe anti-T.B. drug. Anti-bacterial drug therapy is required for all types of active extrapulmonary T.B.

Pulmonary collapse is now in a secondary role.

Pneumoperitoneum can be regulated to reduce lung volume by as much as 25 to 40%. If the pleural space is reasonably free from adhesions, the collapse produced is not limited to the lung bases but is propagated throughout the lung.

Thoracoplasty remains a valuable procedure for the closure of cavities.

Hinshaw, H. C., *Therapeutic Notes*, (Parke, Davis)



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## Errors of Diagnosis in Pediatrics

*A similarity of symptoms in childhood diseases often leads to diagnostic errors; delays in diagnosis may have serious results*

---

BERNARD SCHLESINGER, M.D., London, England

One of the few benefits which a physician gains from advancing years is experience through his mistakes.

Children with a chronic cough, mild fever, anorexia, loss of weight, a debilitated look, and sweating at night are often thought to be tuberculous. Phthisis occurs in childhood only in the rarest circumstances; generally such a case turned out to be an intestinal "mucous disease." Such children have a coated tongue, halitosis, and mucus in the stools. Night sweats are so common in childhood as almost to be physiological.

Otitis media in infants may progress without the usual warnings, and the drum ruptures after a stormy illness. Vomiting and diar-

rhea may have been the predominant feature, fever and leucocytosis may well be absent.

Advanced meningitis may occur before the diagnosis is made. Rapid increase of intracranial pressure is largely avoided by separation of the sutures, so that the classical features of the disease do not arise until late, and various wrong conjunctures are made.

Throughout the centuries teething has been the refuge of doctors who are at a loss to know what is wrong. I have known erysipelas otitis, pyelitis, meningitis and pneumonia to be called teething.

Twice I have seen the lymphocytosis of pertussis labelled leukemia. The implications are so well known to most parents, once made the diag-

nosis is difficult to retract.

Gastroenteritis which fails to improve with modern therapy after a reasonable period should raise a suspicion of celiac or fibrocystic disease.

To miss appendicitis in childhood is particularly serious. The good family doctor has a kind of intuition in regard to this disease, and a specialist who disregards an opinion from that quarter is a foolish man. Too ready administration of antibiotics in doubtful cases can lead to an infected appendix being brought half under control; later it may rupture and produce a pelvic abscess. Diarrhoea may then be one of the main symptoms and, with the tense and tender abdomen, suggest some other abdominal disorder.

The majority of infants who are brought to the doctor with "colic" are suffering from underfeeding, and the trouble is easily remedied.

Rheumatic children seldom complain only of their legs. A serious error is to call osteomyelitis acute rheumatism.

A tic and chorea are continually being confused. No choreic movement is entirely repetitive, or can ever be said to have served a useful purpose.

#### EPILEPSY

A faint should be easy to distinguish from a fit if careful inquiry is made into the circumstances of its occurrence, the aspect of the patient during the attack, and his behaviour afterwards. Breathholding in young children with resultant cerebral anoxia is easily recognized. Real trouble arises in deciding whether a true fit is due to epilepsy or is merely a symptom of some febrile complaint. Some believe that fits can occur only in potential epileptics. The E.E.G. gives some assistance, but one must always be quite convinced before labelling a child an

epileptic.

Some newly-born infants vomit all fluid for the first few days, and are soon thought to have a congenital abnormality of the alimentary tract.

#### INTESTINAL OBSTRUCTION

Abdominal distension and peristalsis are important signs in any form of intestinal obstruction, but are not always obvious, and depend on the position of the lesion. Radiological evidence of pooling of air in the upper part of the gut and its absence at a lower level is sometimes helpful in the diagnosis, but fluid levels can be misleading. If meconium has been freely expelled and there is no bile in the vomit, it is safe to wait. Passage of a rubber catheter into the stomach will exclude oesophageal malformation. An unusual amount of mucus is often found in the vomit; this seems to be the main source of the trouble, which can be remedied by gastric lavage.

Vomiting and headache together are classical features of serious intracranial disease. The possibility of a brain tumor, tuberculous meningitis, or some other serious complaint, must be considered. Migraine and cyclical vomiting should never be diagnosed until renal and cerebral disease have been excluded. With this in view the fundi are to be examined in every such case. Lead-poisoning is rare, but should be noted as likely to give rise to a similar mistake.

An apical systolic murmur is commonly attributed to an organic lesion with little justification. It is a decision that must not be lightly taken; rheumatic carditis is usually diagnosed and the child wrongly condemned to a semi-invalid life. An intense murmur immediately after the first sound, with a fairly wide area of conduction, becoming louder on exercise and heard better with the

child recumbent, is more likely to be due to an organic lesion. Cardiac enlargement, a thrill, and possibly a rheumatic history would be confirmatory evidence.

#### TACHYCARDIA

Paroxysmal tachycardia in infants may masquerade as acute disease of an abdominal viscus. Cardiac failure can rapidly appear, and the enlarged tender liver may give rise to such abdominal rigidity that it cannot be easily palpated. Vomiting may be present and the child show speedy signs of distress. Concentration on the abdomen may result in the tachycardia being overlooked.

Acute enterocolitis of the dysentery group with melaena has to be distinguished from intussusception.

Transient glycosuria may occur after severe vomiting or starvation with resulting ketosis; further urinary tests should therefore be made, especially after the child has been given some sugar, before the probability of diabetes is entertained.

Coli bacilluria commonly gives rise to signs suggesting an acute abdominal condition, and this infection, acute appendicitis, tuberculosis peritonitis and enteric fever have all to be considered.

Urethral valves in boys usually lead to bilateral hydronephrosis and hydroureters, which easily become infected. Sometimes the kidneys are congenitally aplastic. Uremia is the main feature, plus vomiting and an intestinal upset. The enlarged ureters may be mistaken for dilated gut, and the whole clinical picture looks more like some alimentary disorder.

Some cases of incontinence of feces find their way quite wrongly to child guidance clinics; others are diagnosed as Hirschsprung's disease. The rectum is found to be loaded right down to the anus, and feces can often be felt on abdominal pal-

pation. The condition is really a very severe dyschezia due to bad bowel habits, sometimes originating from defecation fears due to pain of an anal abrasion or fissure. Absence of enuresis should exclude any psychological factor.

On the other hand, a case of Hirschsprung's disease may be overlooked in infancy when it presents all the features of lower intestinal obstruction. Most likely disorder with which it is to be confused in the immediate neonatal period is meconium ileus with fibrocystic disease.

The only common blood disease which may lead the doctor astray is leukemia, since it may first appear as a case of serious anemia agranulocytosis, purpura or generalized adenitis; or give rise to bone pains from subperiosteal deposits and be mistaken for rheumatism.

Todd's paralysis after an epileptic fit may persist for a time and cause anxiety in respect of some organic lesion of the central nervous system. "Otitic" or "toxic" hydrocephalus is a mysterious complaint which has often been confused with a brain tumor. No one could be blamed for subjecting a child to ventriculography and even more drastic measures when headache and vomiting with papilloedema are so striking. There may be no localizing signs, but these are not invariably present with a centrally placed neoplasm.

#### STILL'S DISEASE

Still's disease may arise with little or no arthritis, and merely with an irregular undulating fever, a rash and a neutrophil leucocytosis. The possible diagnoses will then be legion. Pericarditis may be present at the onset and rheumatic fever seem the correct diagnosis. Rheumatoid arthritis in childhood may first attack one joint alone. The fever, leucocytosis and toxic state will lead to

fear of a pyogenic arthritis. Still's disease and polyarteritis nodosa run very similar courses.

Bronchiectasis is certainly diagnosed too frequently. If there is a persistent productive cough, steps should always be taken to exclude a chronic sinus infection or segmental pulmonary collapse.

Glandular fever is the other popular diagnosis made on insufficient evidence. If adenitis is confined to the cervical region, tonsillar sepsis is a much more likely cause. Recently we have also been told that a glandular-like fever with eosinophilia, but a negative Paul-Bunnell reaction, may in fact be toxoplasmosis.

#### Hysteria

Finally two warnings. One is against calling a child hysterical until all other possible causes have been excluded. Serious diseases, meningitis, for instance, in children may produce most curious temperamental changes. I was very nearly misled in a case of subacute bacterial endocarditis in an excitable

rheumatic girl of 12 years, who was suddenly struck dumb on seeing her mother after an interval of three weeks. Apart from an old mitral lesion there was nothing to discover. I was sorely tempted to consider the whole affair a hysterical outburst, but somehow refrained from this. There soon followed a right-sided hemiplegia which proved fatal, and the loss of speech was due to a small embolus in Broca's area.

It is easy to place too little significance on clinical features, but one can err in the opposite direction. Children have been confined to bed for months on end for a continued mild fever—"a ninety-niner"—with no symptoms, no signs of leucocytosis, a normal S.R. and all investigations negative. Surely the advice here is to throw the thermometer out of the window and allow the child to get up.

My remarks have probably been of little value. Growing children rarely profit by the mistakes of others; they have to make their own experiences. I wonder if adults are any better, even those who belong to our profession.

### Coronary Heart Disease

Some degree of exercise was recommended. The patient confined to bed should at least move his legs. Others may exercise while going to the commode or may sit in a chair while the nurse makes the bed.

In the acute phase of myocardial infarction smoking should be prohibited. Moderate smoking in the convalescent period does not seem to be harmful.

The physician should stress to patients the nitroglycerin should be used freely for pain and to prevent pain when certain stresses are anticipated. Measures to combat conges-

tive heart failure in its early stages which are advisable, include the use of digitalis and diuretics, and limitation of sodium in varying degrees when indicated. The needless restriction of diet, particularly of sodium, is to be frowned upon. The routine use of quinidine to prevent ventricular fibrillation is not justified.

There is no standard for telling when  $O_2$  is needed, but it will relieve pain in a certain number of patients. Its use in many instances of severe myocardial infarction has saved lives.

R. I. Levy, *Heart Bull.*, 3:117, 1954.

## Causation and Prognosis of Hypertension

*Uncomplicated hypertension is most common, causes little difficulty, and is usually caused by the background and personality of the patient or high salt intake*

---

R. GUBNER, M.D., Brooklyn, New York

Three factors are important for the development of hypertension: familial background, dietary intake of salt, and personality pattern.

The family tendency is well established. The  $\alpha$  factor culture has added is not entirely clear, but there is reason to suspect that it is a heavy salt intake. In large areas of the world where salt intake is small, hypertension is no problem; where the intake is inordinately high, as in Western Europe and the United States, hypertension is prevalent.

The hypertensive patient is likely to have a background of inhibited, hostile, aggressive and competitive attitudes. In most cases there are wide spontaneous fluctuations in blood pressure, a fact which must be borne in mind in appraising ther-

apeutic measures.

In labile hypertension the range is from normal levels (140/90) to definitely elevated levels. This type most often is innocent, and occurs particularly in two types of patients: (1) the apprehensive, or, less commonly, one whose blood pressure rises with emotional stimuli, e.g., merely having the blood pressure taken; (2) an older person with disturbed regulation of sino-aortic, pressor - depressor reflexes, arising from impaired elasticity of the aorta with advancing age. Rarely does this form lead to true hypertensive complications.

In a serial study of 462 hypertensive persons before and after the onset of hypertension, the transition from normal to a consistently ele-

vated blood pressure occurred abruptly in 140 instances. In 94 cases from frequently to consistently elevated blood pressure was observed. In the remaining 228, from normal to frequently elevated blood pressure, which remained in this phase. A large proportion of instances of hypertension had their onset in the 30s and early 40s; few persons have consistent hypertension for the first time at age 55 or older.

The commonest type of hypertension is that of which the patient is unaware and which causes no symptoms, and exists for years before it leads to structural changes.

In a group of insurance applicants with uncomplicated hypertension, blood pressure average 158/98, the annual mortality rate was almost twice the normal. Among a large group of employees observed an-

nually for many years, deaths from cardiovascular causes occurred in 50.8% of normotensive persons; in 60% of those with frequently elevated blood pressure; and in 79.5% of those with consistently elevated diastolic pressure.

Women, although more frequently hypertensive, are not nearly so susceptible to its damaging effects. Hypertension of extreme degree is frequently well tolerated for decades.

In a clinical investigation the mortality rate was 4 times greater among hypertensive patients with evidence of left ventricular strain (inversion of the T wave in lead I) and x-ray evidence of cardiac enlargement, than in hypertensive patients without signs of myocardial disease. Ten-year survival rates were 13% in men, 45% in women.

*The Heart Bulletin* (N.C. Edition) 4:2, 1955.

## AIDS IN DIAGNOSIS

### Mortality Study of Young Diabetic Patients

The average duration of diabetes in patients dying of diabetic coma in the period prior to 1950 was 10 years, and in patients dying of cardiac disease it was 22 years. Kidney disease has been reported as the most important cause of death in juvenile diabetic patients in the past decade, and since 1940, every diabetic child seen in the clinic who has survived 15 or more years of diabetes, and has then come to autopsy, has shown diabetic glomerulosclerosis.

The age-adjusted death rate from diabetes for patients of all ages has remained stationary or has fallen very slightly during the past decade, but morbidity is increasing.

Case histories of 40 fatal cases in a group of 411 juvenile diabetic patients from 1920 to 1950 are presented.

Causes of death included: infection 39.3%; diabetic acidosis 28.6%; kidney disease 10.7%; tuberculosis and accidental death each 7.1%; and hypoglycemia and vascular accident each 3.6%. Infection or diabetic acidosis accounted for the majority of deaths in patients who had diabetes less than 10 years; cardiovascular-renal disease accounted for 40% of the deaths in patients who had diabetes more than 10 years.

The majority of the patients main-

tained fair-to-poor control of their diabetes and had poor social and economic backgrounds.

Autopsy findings indicate that no significant c-v-r pathology occurs in patients who have had poorly controlled diabetes less than 10 years.

Ortmeyer, D. W., et al., *J. Iowa M. Soc.*, 45, 3:137.

### Endoscopic Aids in Diagnosis

*Bronchoscopy* is often useful in cases of cough, hemoptysis, wheeze, bronchial obstruction, bronchitis, bronchiectasis, tracheobronchial tuberculosis and foreign body, as well as benign or malignant tumors of the trachea or bronchi.

*Esophagoscopy* is of value in esophagitis, hiatus hernia, esophageal ulcer, benign stenosis, lye stricture, achalasia, diverticulum, varices, tumor, foreign body, and sometimes in extrinsic pressure, trauma, fistula, pellagra, scleroderma, myasthenia gravis and emotional dysphagia.

*Gastroscopy* should be performed when gastric symptoms persist in spite of negative x-rays; in unexplained hematemesis; in suspected gastritis; and in many cases of gastric ulcer, carcinoma, and lymphoma. No gastroscopic examination can be considered complete without biopsy.

Benedict, E. B., *J. Maine M. A.*, 45:285, 1954.

## Gout

Gout is not a rare malady. It is the suspicion of gout that is rare, not gout itself. The diagnosis of gouty arthritis in the early attacks is usually easy on the local latures, increased serum uric acid, and response to adequate colchicine.

Points that are helpful are family history of gout, acute arthritis in men over 40, patient appears wearing a shoe cut out over the 1st metatarsophalangeal joint, x-ray appearance and urate calculi.

Onset is sudden, in half the cases the initial joint will be the 1st metatarsophalangeal. In a few hours it will swell, become extremely tender, hot and dusky red. Other joints that may be involved initially are ankle, knee, instep, heel, elbow or the small joints of the hands or wrist. The initial attack lasts 3 to 10 days unless prompt treatment is instituted. Complete return of function is usual. There may be GI discomfort, fever to 101-102 and a moderate leukocytosis.

The between-attacks stage may last for years, interspersed by occasional acute attacks.

In acute attacks bed rest, liberal use of analgesics, and a trial of hot or cold compresses. Forced fluids.

As specific therapy colchicine has been the drug of choice, now ACTH and Butazolidin may equal or surpass colchicine in acute attacks. ACTH gel 80 to 100 mg. daily for 2 to 3 days will terminate many, then it is usually possible to taper off the dosage, concurrently giving colchicine 1 or 2 mg. daily. Colchicine alone is given orally in doses of 1.0 mg. every 2 hours until the attack subsides or diarrhea, nausea or vomiting ensues. Usually the total dosage will be 6 to 8 mg.

Because of its toxicity Butazolidin should be used with caution. In future attacks the patient will respond to the same dosage. To prevent at-

tacks 0.5 to 1.0 mg. colchicine daily may serve. Benemid has recently come to the front for long term prophylactic use in doses of 0.5 to 1.0 gm. daily. Used along with salicylates, its effects are nullified.

Drastic curtailment of purine intake is *inadvisable*. Small amounts of meats, and seafood, and alcohol may be allowed.

McClelland, R. L., *Kentucky M. J.*, 53, 2:120-123, 1955.

## Obstruction of the Renal Artery Producing Malignant Hypertension

A 34-year-old dairy worker admitted March 10, 1953, complaining of pain in the head, easy tiring, loss of appetite, loss of 40 pounds, and vomiting. One year previously b.p. report normal. One month before entry symptoms began; just before admission severe occipital headaches and pain into the back of the neck.

B.P. 195/130; grade 3 hypertensive retinopathy, heart sounds regular and normal; no murmurs detectable. March 10 to 20, b.p. 170/110 to 210/150. Urine 1.004, 4-plus albumin. Blood urea N. 35 mg. per 100 cc., max. sp. gr. concentration 1.013. IV urogram showed very poor function of the r. kidney. An aortogram showed a normal l. renal artery and blood supply to l. kidney. On the r. the renal artery was deformed at the hilus of the kidney.

At operation, 10 d. later, many fibrous bands were seen binding the artery to the vein, and having kinked the artery to an S turn. Pulsations distal to this point were diminished. The kink in the renal artery could not be entirely freed.

One hour after operation b.p. was 110/80, and on the evening fell as low as 98/66. Postoperative course was uneventful and the b.p. stabilized about 130/70. 8th postop. day



*Severe chronic cystic acne of face, neck, and shoulders in 18 year old male; treatment based on diet, x-ray, vitamins, and vaccines unsuccessful over 5 year period.*

*Following 4 months of treatment with "Premarin" Lotion on face and neck, infection and cysts have cleared. Untreated shoulders show no improvement.*



## Refractory cases of acne vulgaris

### **respond to "Premarin"® Lotion**

Conjugated Estrogens (equine) for topical application

A highly gratifying response, as in the patient shown above, was achieved with "Premarin" Lotion in 70 to 80 per cent of patients of both sexes with acne vulgaris that had failed to respond to other therapy.<sup>1</sup> "Premarin" Lotion is easy to apply; permits dosage control to eliminate possibility of side effects; is esthetically acceptable to both male and female patients.

#### **also effective in seborrheic alopecia**

In another series of patients, scaling, itching, and falling hair (particularly about the vertex of the scalp) were controlled within three to six weeks by the application of "Premarin" Lotion two or three times daily.<sup>2</sup> No systemic effects were noted.

Supplied: No. 875 — Bottles of 60 cc. (1 mg. per cc.) with applicator.

*Detailed information available upon request.*

1. Shapiro, I.: Postgrad. Med. 15:503 (June) 1954; J. M. Soc. New Jersey 52:6 (Jan) 1955.
2. Shapiro, I.: J. M. Soc. New Jersey 50:17 (Jan.) 1953.

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the ophthalmologist reported improvement in the retinopathy. 3 days after operation the blood urea N was 41 mg. per 100 cc. On discharge 8 days post op. only a trace of albumin in the urine; the blood urea N 22 mg.

Despite bilaterally diminished renal function, removal of the offending kidney, which pathological examination showed to be normal, effected a "cure" of the hypertensive state by the most rigid criteria. The value of abdominal aortography in identifying the vascular defect is again demonstrated. This case provides further evidence that a diminished blood flow in a major renal artery may cause hypertension and impairment of total renal function.

Imber, Irving, et al., *New England J. Med.*, 252:301-304, 1955.

### Retrobulbar Neuritis and Multiple Sclerosis

An episode of acute retrobulbar neuritis is generally recognized as a possible primary symptom of multiple sclerosis. What is the frequency with which multiple sclerosis develops after such an episode? Of 87 patients followed for 10 to 15 years after an initial attack of acute retrobulbar neuritis of undetermined cause, 28 (32.2%) showed evidence of multiple sclerosis at a later date; 26 were between 20 and 44 years of age at the time of the initial attack.

Our data indicate that a person of this age group who has an attack of acute retrobulbar neuritis has a 40 to 50% chance of having multiple sclerosis develop within 10 to 15 years. In the cases in which retrobulbar neuritis occurs before the age of 20 years, the chance of multiple sclerosis appearing is less likely, and when it occurs after the age of 44 years, the chance is remote.

Taub, R. G., et al., *Proc. Staff Meet. Mayo Clin.*, 29:364, 1954.

## NEW PHARMACEUTICAL PRODUCTS

### Tedral Suspension

(Warner-Chilcott)

An anise-mint flavored suspension containing 2 gr. theophylline, 3/8 gr. ephedrine and 1/8 gr. phenobarbital in each teaspoonful. The drug combines bronchiole-dilating activity with anti-congestive action and moderate sedation. *Indications:* symptomatic relief of asthma for adults and children unable to swallow tablets. *Supplied:* bottles of 4 fluid ounces.

### Piperat Tartrate

(Lincoln)

Oxyuricide and ascaricide for treatment of pinworm and roundworm in children and adults. Essentially atoxic in recommended dosage. *Indications:* treatment of oxyuriasis and ascariasis. Enemas, purges, fasting not required. *Dosage:* 1 to 9 tablets daily depending on weight. *Supplied:* bottles of 200 and 1000 double scored tablets.

### Colostat

(Schenley)

Each fluid ounce contains 6.0 gm. colloidal kaolin, 0.75 gm. calcium carbonate and 0.6 gm. sodium carboxymethylcellulose. *Indications:* management and treatment of diarrhea and other inflammatory conditions of the bowel and intestinal infections. *Administration:* orally. *Dosage:* 1 to 2 tablespoonsfuls after each bowel movement. *Supplied:* 1 pint dispensing bottles.

### Tronolen Lotion

(Abbott)

An anesthetic, flesh-toned topical preparation containing 1% tronothane hydrochloride and 2% di-paralene hydrochloride. *Indications:* surface pain or itching in various dermatoses, pruritic syndromes, minor burns or sunburn, poison ivy, oak or sumac, insect bites, athlete's foot, abrasions, chafing, diaper rash, scalds. *Administration:* 3 or 4 times daily or as directed by the physician. *Supplied:* in 75 cc. plastic squeeze bottles.

### Cobasal

(Rand)

Each 2 tablets contain 0.125 gm. of dipyrrone, 8 gr. para-amino benzoic acid, 6 gr. salicylamide and 5 mcg. of vitamin B<sub>12</sub>. *Indications:* arthritis and allied conditions. *Administration:* orally. *Dosage:* 2 tablets every 4 hours. *Supplied:* bottles of 100 and 1000.

### Ceniron

(Central)

Oral hematinic—each tablet contains 200 mg. of ferrous sulfate, exsiccated, 125 mg. of ascorbic acid, 12 mg. of manganese sulfate monohydrate, 3 mg. of copper sulfate and 0.4 mg. of cobalt chloride hexahydrate. *Indications:* iron - deficiency anemias. *Supplied:* bottles of 100, 500 and 1000 tablets.

**Butibel**

(McNeil)

Provides balanced antispasmodic-sedative medication. Each tablet or 5 cc. contains 10 mg. of Butisol sodium and 15 mg. of ext. belladonna. *Indications:* acute and chronic diarrhea, acute gastroenteritis, ulcerative colitis, regional enteritis and dysenteries, peptic ulcer and dyspepsia. *Administration:* orally. *Dosage:* as directed by physician. *Supplied:* bottles of 100 and 1000 tablets and elixir in pints and gallons.

**Acidiron**

(Walker)

Each green tablet contains 3 grains of ferrous sulfate, excised and 125 mg. of hydrochloric acid, diluted. *Indications:* iron deficiency anemias in older patients with hypochlorhydria. *Dosage:* 1 or 2 tablets followed by a glass of water after meals. *Supplied:* bottles of 100.

**Otamylon**

(Winthrop-Stearns)

Bactericidal, fungicidal, analgesic, hygroscopic ear drops containing 5% Sulfonyl hydrochloride and 5% benzocaine in propylene glycol. *Indications:* acute and chronic otitis externa, furunculosis, acute and chronic otitis media, after mastoidectomy and fenestration operations. *Administration:* (1) patient lying on the non-affected side, 2 or 3 drops are instilled into the ear canal, then plugged with sterile cotton. (2) Alternate method is to insert a gauze wick moistened with the preparation into the external ear canal.

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**Cevicetyl** (Chicago Pharmacal)

Each tablet contains 325 mg. of aspirin and 125 mg. of ascorbic acid (vitamin C). Relieves pain and reduces fever without depleting the system of vitamin C. *Indications:* if administered in the early stages of the common cold, whooping cough or measles, the more severe stages of same are prevented from occurring. *Administration:* orally. *Dosage:* 2 tablets q.i.d. in acute stages and 1 tablet 3 times daily thereafter. *Supplied:* bottles of 100 and 1000.

**Cortril Vaginal Tablets** (Pfizer)

Each shaped tablet contains 10 mg. of Cortril (hydrocortisone) in a special carbo-wax base. *Indications:* nonspecific vaginitis, neuro-dermatitis involving the vagina and as adjunct to the specific treatment of senile vaginitis and infections such as monilial and trichomonal vaginitis. *Administration:* one tablet is inserted once or twice daily until symptoms subside. *Supplied:* individually wrapped in foil, 5 tablets to a strip, 2 strips to a carton.

## LITERATURE SERVICE

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	p. 855	me
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### Rheumatoid Arthritis

Cortisone is contraindicated in edema, peptic ulcer history, renal or hepatic damage, hypertension, psychoses, and tuberculosis or other infectious disease.

Cortisone is beneficial in arthritis where other methods fail. Occasionally a sustained remission is obtained. Side effects are directly related to size of dose. A carefully controlled study finds no apparent difference between long-term cortisone or aspirin therapy. The contraindications for oral hydrocortisone are the same as for cortisone. Treatment with oral hydrocortisone is 25-50% more effective than with cortisone, side effects are less as required dose is smaller. Hydrocortisone (intra-articular)—contraindications in doses of over 35 mg. same as with cortisone. Results are only temporary. Side effects are lowered; disappear from the synovial cavity in a few hours. Effects due to systemic reactions rather than to any local activity.

Intravenous typhoid vaccine is contraindicated in marked debility arteriosclerosis. Subjective improvement frequent; thought to be by stimulation of the adrenal cortex.

Umbilical Cord Serum contraindicated in Rh negativity, dangers of contaminated serum or plasma (infectious hepatitis). A high percent-

age of sustained remissions.

Placental extract, no contraindications. Sustained remissions are obtained frequently.

Therapy of rheumatoid arthritis is initially, conservative management by application of the measures long in use. If they prove inadequate these more specific substances may be employed.

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Dillon, R. N., et al., *Northwest Med.* 54, 11:156-161, 1955.

### Recent Advances in the Treatment of Poliomyelitis

The mortality rate has been reduced by increased use and understanding of tracheotomy and mechanical respirators of various types; by improved treatment of complications such as pneumonitis and atelectasis with antibiotics, trypsin, nebulization, and mechanical coughing devices; and by the development of local professional teams in smaller communities. There has been great improvement in techniques and devices for restoration of function, such as glossopharyngeal breathing, muscle transplants, functional bracing, and prostheses. Programs have been developed to send patients who must use respirators to their homes with adequate support to insure all of the advantages of the hospital, plus those inherent in the home situation.

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Affeldt, J. E., *J.A.M.A.*, 156:12, 1954.

## The Prevention of Rheumatic Fever by the Use of Antibiotics

Aureomycin reduces the incidence of rheumatic sequelae somewhat less effectively than penicillin. Aureomycin, 2 gm. daily for 7 days, is given patients sensitive to penicillin.

In streptococcal pharyngitis best results are obtained when treatment is initiated within 48 hours of symptoms of sore throat; but treatment instituted even as late as 9 days after the onset of symptoms of sore throat may exert some prophylactic effect.

The major limitation of this approach to the prevention of rheumatic fever is the difficulty of clinical diagnosis of streptococcal sore throat. Penicillin should not be given promiscuously to patients with viral upper-respiratory infections. Simple coryza, hoarseness and tracheitis are rarely due to streptococci. The syndrome of sudden onset of fever, sore throat, beefy redness of the pharynx and pharyngeal exudate suggests the diagnosis. Evidence of cervical lymphadenitis and the presence of leukocytosis lend further support to it. With experience a proper diagnosis of streptococcal pharyngitis can be made on clinical criteria alone with 70% accuracy.

Because the preceding streptococcal infection may be inapparent in at least 38% of patients who develop rheumatic fever, it is obvious that the chemotherapeutic approach will prevent, at best, little more than half of the total cases. Proper diagnosis and treatment may reduce prevalence of streptococcal infections and this could be reflected in a significant decline in the incidence of rheumatic fever.

Pending more knowledge and a better approach, the incidence and morbidity of the disease can be reduced significantly by an apprecia-

tion on the part of physicians and the general public of the importance of early diagnosis and proper therapy of streptococcal disease, and upon the diligent protection of rheumatic subjects from streptococcal infection.

Stoller, G. H., *Bull. New York Acad. Med.*, 31:165-179, 1955.

## Annual Report on Surgery of Stomach and Duodenum

A recent study reveals: (1) that vagotomy can give excellent results in 70% of cases of gastrojejunal ulcer which has developed after removal of at least 3/4 of the stomach, whereas results after resection of the stomach were satisfactory in only 50% of the patients in this group; (2) that gastric resection was followed by an excellent result in 86.5% of patients whose ulcer developed after gastroenterostomy, and that vagotomy produced excellent results in 77.8% of a similar group of patients.

Partial gastrectomy was performed in 724 patients in 1953. In 605 cases this operation was carried out for a benign type of condition with 9 deaths (1.5%); in the remaining 119 cases for a malignant lesion with 6 deaths (5.0%).

Priestley, J. T., *Proc. Staff Meet. Mayo Clin.*, 29:638, 1954.

## Use of Erythromycin in Diphtheria

Erythromycin, 800 mg. daily by mouth in 4 divided doses for 6 days, appears to be effective in rapidly clearing diphtheria organisms from the throat. Erythromycin is advocated as an adjunct and not as a substitute for antitoxin in acute diphtheria.

Blute, Jr., L. F., *New England J. Med.*, 251:70, 1954.

## Mephate in Back Injuries

A skeletal-muscle relaxant with a central nervous-system sedative effect (Mephate, Robins) brought satisfactory relief in 86.8% of 91 successive cases of injured lower backs. After a new back program was instituted among 17,860 employees of a manufacturing company, during a 3-month period, out of 236 total days lost, only 3 days lost were attributable to back injuries. Before the program started, out of a total of 244 days lost in a comparable period, 87 were due to back injuries. In addition to the use of Mephate, a course of simple exercises designed to keep the muscles flexible and relaxed was carried out.

Jesup, Robert, et al., *Am. Pract.*, 5:792, 1954.

## Treatment of Incapacitated Euthyroid Cardiac Patients With Radioactive Iodine

Hypothyroidism can be regularly induced in euthyroid patients by one or more doses of radioactive iodine. After such treatment in 50 clinics of 1,070 patients with intractable angina pectoris or congestive failure, 75% of the 720 patients with angina pectoris showed worth-while improvement (half marked improvement and half a good result); and 60% of the 350 patients with congestive failure showed worth-while improvement (20% marked and 40% moderate). These patients were given small daily doses of thyroid to maintain the lowest metabolic rate consistent with comfort.

In intractable cardiac cripples who are usually considered for surgical treatment, hypothyroidism induced by radioactive iodine gives improvement through medical means without the risk and complications of surgery.

Blumgart, H. L., et al., *J.A.M.A.*, 157:1, 1955.

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## Epilepsy

Suppression of epileptic manifestations with minimal impairment of efficiency is best achieved by skilful use of antiepileptic drugs. Ketogenic diet is seldom used.

Recent summaries agree on effectiveness of Dilantin and phenobarbital and its homologue, Mebaral, singly or in combination; they vary in their enthusiasm for bromides. Some find them useful in children whose convulsions are secondary to brain damage, and for patients whose convulsive attacks cannot be controlled by other methods.

Mesantoin, a homologue of Dilantin, is helpful against convulsive and psychomotor seizures; dosage one or two 0.1 gm. tablets a day for a child, and up to six or eight 0.1 gm. tablets for adults. The dosage is limited by sedative effect. Mesantoin is sometimes effective for patients who do not respond to Dilantin, or who have severe hyperplasia of the gums. It holds threat of thrombocytopenia or neutropenia or even aplastic anemia, and because of the necessity for monthly blood counts, it is more troublesome to use than Dilantin. A rash, fever or lymphadenopathy in the first 8 to 10 days requires withdrawal.

Mysoline is reported effective against convulsive and psychomotor seizures, ineffectual against petit-mal seizures. Because dizziness and sedative effects initially may be troublesome, a portion of a tablet, 50 to 100 mg., is given once a day for several days, with increase in dosage to match gain in tolerance. No liver, bone-marrow or kidney toxicity has been reported. Average daily prescription for young children is 125 mg., t.i.d.; that for adults up to 500 mg. 3 or 4 times a day.

Phenurone is anticonvulsant, and effective against psychomotor and petit-mal seizures. It is not the drug of choice because, in rare cases, it causes toxic reactions of the liver

or bone marrow and tends to aggravate pre-existent personality disorders in some patients.

Tridione is the standard against which other anti-petit mal medicines are measured—0.6 to 0.9 gm daily for a child, and 1.2 gm. for an adult—limited by excessive sedation and requires monthly blood examinations. Paradione, a homologue of Tridione, is similar in its effects and dosage. Depression of the blood has been less commonly reported, and the drug is sometimes effective when Tridione fails.

In 300 cases we have found Milontin potent against petit-mal attacks. Although it is not as regularly helpful as the diones, we prefer it because of its freedom from toxic effects on the blood.

Diamox is an effective suppressor of petit-mal attacks. Patients whose electrograms respond excessively to overbreathing are most likely to benefit. There is no advantage in giving more than three 250 mg. tablets a day, and from this dosage no toxic side effects have been observed.

Atabrine, 0.1 to 0.4 gm. a day, is useful against petit-mal attacks, and except for yellow skin is free from toxicity.

A number of homologues of Dilantin, Tridione and phenobarbital, and several new treatment drugs are undergoing evaluation in this country and abroad.

Davidson, Jr., D. T., *New England J. Med.*, 251:89, 1954.

## Piperazine in Treatment of Roundworm

Sixteen children were treated with piperazine adipate, all save one appeared cured. No subsequent appearance of worm in the feces, and complete disappearance of the presenting symptoms. Dosage 1 tablet per day for each year of life up to 6. Over 6 years, 2 tablets 3 times a day, continued for one week.

Rearden, James., *Brit. M. J.*, 4:872-892, 1954.

## BOOK REVIEWS

### **The Bane of Drug Addiction**

by Orin Ross Yost, M.D., Fellow of the American Psychiatric Association. The Macmillan Company, New York. 1954

The book deals with the underlying and the ostensible causes of drug addiction, has chapters on: What are the Addicting Drugs? Who are the Drug Addicts? Drug User or Drug Addict? A Typical Drug Addict, Treatment for Drug Addiction, and Controlling the Drug Traffic.

The subject is covered satisfactorily and the appended glossary will prove helpful.

### **Pediatric Diagnosis**

Morris Green, M.D. and Julius B. Richmond, M.D. W. B. Saunders Company, Philadelphia and London. 1954. \$10.00

The dedication, "To those who care for children everywhere," has a strong appeal, and predisposes the reader in favor of the book. As one goes on he is more and more impressed with the usability of the book in the hands of those to whom it is dedicated. Emphasis is placed on the taking of a truly individual history in each case, and on the value of observation during home visits. It is needless to call special attention to any of the detailed teaching. The whole book is excellent.

### **Collected Papers of the Mayo Clinic and the Mayo Foundation**

edited by Richard B. Hewitt, B.A., M.A., M.D.; et al. Vol 46, 1954. W. B. Saunders Co., Philadelphia. London. 1955. \$12.50

We are told that the material for the present volume has been selected primarily with the interests of the general practitioner, the general surgeon and the diagnostician in mind. Also, it has been deemed essential to include material representative of the specialties and of the basic sciences. From every article included every unnecessary word has been deleted. A great many papers are "by title and reference only." The presentations have the 4 essentials — authoritativeness, adequacy, clarity, and brevity.

### **Management of Addictions**

edited by Edward Podolsky, M.D., Department of Psychiatry, Kings County Hospital, Brooklyn, N. Y. Philosophical Library, Inc., 15 E. 40th St., New York 16, N. Y. 1955. \$7.50

Three parts of the book deal with alcoholics, one part with drug addictions. In the book one may find the conceptions as to nature, diagnosis, prognosis and treatment methods of more than half a hundred teachers and therapists in this field all the way from India to California, and from Connecticut to Texas — surely a wide enough choice.

### A Textbook of Physiology

edited by John F. Fulton, M.D.,  
Sterling Professor of the History of  
Medicine, Yale University School of  
Medicine, 17th edition, illustrated.  
W. B. Saunders Company, Philadelphia  
and London. 1955. \$13.50

It is most likely that, of all the pre-clinical studies to which the medical student is exposed, physiology is the most neglected in the years after graduation. Sampling here and there in this textbook, this reviewer is mildly astonished at seeing how few additions have been made to what is *known* of physiology, since he sat under a professor of physiology more than two score years ago.

Practitioners who will buy this book and make use of it will add greatly to their usefulness to their patients, and it will give them a stick with which wherewith to crack the head of many a garrulous drug salesman and many a pompous speaker on subjects medical.

### Peripheral Vascular Diseases

Edgar V. Allen, M.D., F.A.C.P.,  
Nelson W. Barker, M.D., F.A.C.P.,  
and Edgar A. Hines, Jr., M.D.,  
F.A.C.P. Second edition, 316 illustrations,  
7 in color. W. B. Saunders Company,  
Philadelphia and London 1955. \$13.00

This book is largely an account of the work of the authors and their colleagues of the Mayo Clinic over the past quarter-century. Every doctor has at least a superficial acquaintance with this work and some realization of its importance. A great number of disease conditions are appropriately included which few of us would think of first as peripheral vascular diseases. The sections on treatment, medical and surgical, should go far to bring order out of the confusion which has been brought about by the great diversity of claims made by those regarded as authorities in the field.

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